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Clinical Immunology 53/8 (725-730) 1998.

Advances in Experimental medicine and biology 409: 61-73; 1996

Clinical and experimental allergy 28⊗11): 1374-1383; Nov 1998

J. Allergy and clinical immunology 101(4 pt 1): 521-30; April 1998

Immunology 87(1): 119-26; Jan 1996

British J of Pharmacology 115(7): 1141-8, Aug 1995

J experimental medicine 178(1): 349-353; July 1993

J immunology 147(8): 2455-2460; 1991

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Scandinavian Journal of Clinical and Laboratory Investigation, Supplement 51/204 (17-31) 1991.

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Clinical Immunology 53/8 (725-730) 1998.

Advances in Experimental medicine and biology 409: 61-73; 1996

Clinical and experimental allergy 28⊗11): 1374-1383; Nov 1998

J. Allergy and clinical immunology 101(4 pt 1): 521-30; April 1998

Immunology 87(1): 119-26; Jan 1996

British J of Pharmacology 115(7): 1141-8, Aug 1995

J experimental medicine 178(1): 349-353; July 1993

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L2 ANSWER 1 OF 50 MEDLINE DUPLICATE 1
2001217686 Document Number: 21176192. PubMed ID: 11277829. Detection of peanut allergens in breast milk of lactating women. Vadas P; Wai Y; **Burks W**; Perelman B. (Division of Allergy and Clinical Immunology, St Michael's Hospital, Room 8-161, Victoria Wing, 30 Bond St, Toronto, Ontario, Canada M5B 1W8.. pv4588@home.com) . JAMA, (2001 Apr 4) 285 (13) 1746-8. Journal code: KFR; 7501160. ISSN: 0098-7484. Pub. country: United States. Language: English.
AB CONTEXT: Most individuals who react to peanuts do so on their first known exposure. A potential but unproven route of occult exposure resulting in sensitization to peanut is via breast milk during lactation. OBJECTIVE: To investigate the ability of maternal dietary peanut protein to pass into breast milk during lactation. DESIGN AND SETTING: Clinical investigation conducted at 2 North American hospitals from March 1999 to October 2000. PATIENTS: Twenty-three healthy, lactating women aged 21 to 35 years. INTERVENTION: Each woman consumed 50 g of dry roasted peanuts, after which breast milk samples were collected at hourly intervals. MAIN OUTCOME MEASURES: Presence in breast milk of total peanut protein, analyzed by a sandwich enzyme-linked immunosorbent assay, and 2 major peanut allergens, Ara h 1 and Ara h 2, detected by immunoblot analysis. RESULTS: Peanut protein was detected in 11 of 23 subjects. It was detected in 10 subjects within 2 hours of ingestion and in 1 subject within 6 hours. The median peak peanut protein concentration in breast milk was 200 ng/mL (mean, 222 ng/mL; range, 120-430 ng/mL). Both major peanut allergens Ara h 1 and Ara h 2 were detected. CONCLUSIONS: Peanut protein is secreted into breast milk of lactating women following maternal dietary ingestion. Exposure to peanut protein during breastfeeding is a route of occult exposure that may result in sensitization of at-risk infants.

L2 ANSWER 2 OF 50 MEDLINE DUPLICATE 2
2001195305 Document Number: 21101561. PubMed ID: 11174206. The natural history of peanut allergy. Skolnick H S; Conover-Walker M K; Koerner C B; Sampson H A; **Burks W**; Wood R A. (Department of Pediatrics, Johns Hopkins University, Baltimore, Md, USA.) JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, (2001 Feb) 107 (2) 367-74. Journal code: H53; 1275002. ISSN: 0091-6749. Pub. country: United States. Language: English.
AB BACKGROUND: It has traditionally been assumed that peanut allergy is rarely outgrown. OBJECTIVE: The goal of this study was to determine the number of children with peanut allergy who become tolerant of peanut. METHODS: Patients aged 4 to 20 years with a diagnosis of peanut allergy were evaluated by questionnaire, skin testing, and a quantitative antibody

fluorescent-enzyme immunoassay. Patients who had been reaction free in the past year and had a peanut IgE (PN-IgE) level less than 20 kilounits of antibody per liter (kU(A)/L) were offered an open or double-blind, placebo-controlled peanut challenge. RESULTS: A total of 223 patients were evaluated, and of those, 85 (PN-IgE < 0.35-20.4 kU(A)/L [median 1.42 kU(A)/L]) participated in an oral peanut challenge. Forty-eight (21.5%) patients had negative challenge results and were believed to have outgrown their peanut allergy (aged 4-17.5 years [median 6 years]; PN-IgE < 0.35-20.4 kU(A)/L [median 0.69 kU(A)/L]). Thirty-seven failed the challenge (aged 4-13 years [median 6.5 years]; RAST < 0.35-18.2 kU(A)/L [median 2.06 kU(A)/L]). Forty-one patients with PN-IgE levels less than 20 kU(A)/L declined to undergo challenge, and 97 were not eligible for challenge because their PN-IgE levels were greater than 20 kU(A)/L or they had had a recent reaction. Sixty-seven percent of patients with PN-IgE levels less than 2 kU(A)/L and 61% with levels less than 5 kU(A)/L had negative challenge results. Of those who underwent challenge, PN-IgE levels for those who passed versus those who failed were different at the time of challenge (P = .009), but not at the time of diagnosis (P = .25). CONCLUSION: This study demonstrates that peanut allergy is outgrown in about 21.5% of patients. Patients with low PN-IgE levels should be offered a peanut challenge in a medical setting to demonstrate whether they can now tolerate peanuts.

L2 ANSWER 3 OF 50 SCISEARCH COPYRIGHT 2001 ISI (R) DUPLICATE 3
2001:200724 The Genuine Article (R) Number: 405RE. Crohn's disease in X-linked agammaglobulinemia. Frazer D H (Reprint); Williams L W; **Burks W**. Duke Univ, Durham, NC USA; Arkansas Childrens Hosp, Little Rock, AR 72202 USA. JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY (FEB 2001) Vol. 107, No. 2, Supp. [S], pp. S203-S203. MA 671. Publisher: MOSBY, INC. 11830 WESTLINE INDUSTRIAL DR, ST LOUIS, MO 63146-3318 USA. ISSN: 0091-6749. Pub. country: USA. Language: English.

L2 ANSWER 4 OF 50 SCISEARCH COPYRIGHT 2001 ISI (R) DUPLICATE 4
2001:200516 The Genuine Article (R) Number: 405RE. Comparison of Chinese and American cooking methods on allergenicity of peanut. Morrow E (Reprint); Beyer K; Grishina G; Bannon G A; **Burks W**; Sampson H A. Mt Sinai Sch Med, New York, NY USA; Univ Arkansas, Sch Med, Little Rock, AR USA. JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY (FEB 2001) Vol. 107, No. 2, Supp. [S], pp. S139-S139. MA 460. Publisher: MOSBY, INC. 11830 WESTLINE INDUSTRIAL DR, ST LOUIS, MO 63146-3318 USA. ISSN: 0091-6749. Pub. country: USA. Language: English.

L2 ANSWER 5 OF 50 SCISEARCH COPYRIGHT 2001 ISI (R) DUPLICATE 5
2001:200517 The Genuine Article (R) Number: 405RE. Role of conformational and linearized epitopes in the achievement of tolerance in peanut allergy. Ellman L K (Reprint); Beyer K; Bardina L; Jarvinen K M; Bannon G A; **Burks W**; Sampson H A. Mt Sinai Sch Med, New York, NY USA; Univ Arkansas, Sch Med, Little Rock, AR USA. JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY (FEB 2001) Vol. 107, No. 2, Supp. [S], pp. S139-S139. MA 461. Publisher: MOSBY, INC. 11830 WESTLINE INDUSTRIAL DR, ST LOUIS, MO 63146-3318 USA. ISSN: 0091-6749. Pub. country: USA. Language: English.

L2 ANSWER 6 OF 50 SCISEARCH COPYRIGHT 2001 ISI (R) DUPLICATE 6

2001:200256 The Genuine Article (R) Number: 405RE. Characteristics and progression of allergic reactions to peanuts. Skolnick H S (Reprint); Conover-Walker M K; Koerner C B; Sampson H A; **Burks W**; Wood R A. Johns Hopkins Hosp, Baltimore, MD 21287 USA; Mt Sinai Hosp, New York, NY 10029 USA; Arkansas Childrens Hosp, Little Rock, AR 72202 USA. JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY (FEB 2001) Vol. 107, No. 2, Supp. [S], pp.
S58-S58. MA 199. Publisher: MOSBY, INC. 11830 WESTLINE INDUSTRIAL DR, ST LOUIS, MO 63146-3318 USA. ISSN: 0091-6749. Pub. country: USA. Language: English.

L2 ANSWER 7 OF 50 MEDLINE DUPLICATE 7
2001069753 Document Number: 20534828. PubMed ID: 11080722. Randomized, double-blind, crossover challenge study in 53 subjects reporting adverse reactions to melon (Cucumis melo). Rodriguez J; Crespo J F; **Burks W**; Rivas-Plata C; Fernandez-Anaya S; Vives R; Daroca P. (Servicio de Alergia, Hospital Universitario Doce de Octubre, Madrid, Spain.) JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, (2000 Nov) 106 (5) 968-72. Journal code: H53. ISSN: 0091-6749. Pub. country: United States. Language: English.
AB BACKGROUND: Few studies have evaluated IgE-mediated hypersensitivity to melon with details of clinical reactions confirmed by double-blind, placebo-controlled, food challenges (DBPCFCs). OBJECTIVE: We sought to investigate clinical features (type and severity of reactions, age at onset, results of skin prick and in vitro tests, and incidence of other allergic diseases and associated food allergies) of acute allergic reactions to melon confirmed by DBPCFCs. METHODS: Fifty-three consecutive adult patients complaining of adverse reactions to melon were included in the study. Skin prick tests and detection of specific IgE were performed in all patients with melon, avocado, kiwi, banana, chestnut, latex, pollen, and other offending foods. Patients first underwent an open food challenge, unless they had a convincing history of severe anaphylaxis. Positive open food challenge reactions were subsequently evaluated by DBPCFCs. RESULTS: Actual clinical reactivity was confirmed in 19 (36%) of 53 patients. The most frequent symptom was oral allergy syndrome (n = 14),
but two patients experienced life-threatening reactions, including respiratory symptoms and hypotension. The positive predictive value for a skin prick test was 42%, and that for specific IgE measurement was 44%. Forty-five reactions to 15 other foods were confirmed in 18 patients. The most common foods associated with melon allergy were avocado (n = 7), banana (n = 7), kiwi (n = 6), watermelon (n = 6), and peach (n = 5). Onset
of melon-induced allergic symptoms occurred from 6 to 45 years (median, 20
years), preceded by seasonal rhinitis, asthma, or both in 88% (15/17). CONCLUSION: About one third of reported reactions to melon are confirmed by means of DBPCFC, which has been proven to be the most reliable procedure in the diagnosis of clinical fruit allergy. Isolated melon allergy is rare, with most patients either having allergic rhinitis, asthma, or both and associated food allergies.

L2 ANSWER 8 OF 50 MEDLINE DUPLICATE 8
2001122889 Document Number: 21015905. PubMed ID: 11131941. Diagnosis of allergic reactions to food. **Burks W**. (University of Arkansas for Medical Sciences, Arkansas Children's Hospital, Little Rock, Arkansas, USA.) PEDIATRIC ANNALS, (2000 Dec) 29 (12) 744-52. Ref: 19. Journal code: OUB. ISSN: 0090-4481. Pub. country: United States. Language: English.

L2 ANSWER 9 OF 50 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.DUPLICATE 9
2000433049 EMBASE Esophageal candidiasis in an infant with reflux esophagitis. Uc A.; North P.; **Burks W**.. Dr. A. Uc, Univ. of Iowa

Hospitals and Clinics, 2865 JPP, Department of Pediatrics, 200 Hawkins Drive, Iowa City, IA 52242, United States. Journal of Pediatric Gastroenterology and Nutrition 31/5 (572-574) 2000.
Refs: 12.
ISSN: 0277-2116. CODEN: JPGND6. Pub. Country: United States. Language: English.

L2 ANSWER 10 OF 50 CAPLUS COPYRIGHT 2001 ACS
1999:594994 Document No. 131:227660 Tertiary structure of peanut allergen Ara h 1. **Burks, Wesley, Jr.**; Helm, Ricki M.; Cockrell, Gael; Bannon, Gary A.; Stanley, J. Steven; Shin, David S.; Sampson, Hugh; Compadre, Cesar M.; Huang, Shau K. (Board of Trustees of the University of Arkansas, USA). PCT Int. Appl. WO 9945961 A1 19990916, 193 pp.
DESIGNATED STATES: W: AE, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US5494 19990312.
PRIORITY: US 1998-PV77763 19980312.
AB Ara h 1, a major peanut allergen, has been isolated and shown to contain 23 linear IgE-binding epitopes, 6-10 residues in length. Anal. of wild-type and mutant peptides with single amino acids substitutions showed that amino acids residing in the middle of the epitope were more crit. for IgE binding; that polar charged residues occurred more frequently within the epitope while apolar residues were more important for IgE binding; and that a single amino acid substitution in an epitope resulted in a loss of ability to bind IgE. In addn., a homol.-based mol. model of the Ara h 1 protein representing residues 171-586 was made and allowed visualization of epitopes 10-22. The majority of these epitopes appear clustered and many of the crit. amino acids involved in binding are evenly distributed on the surface. The information from the mutational anal. and the mol. model will aid in the design of immunotherapies.

L2 ANSWER 11 OF 50 SCISEARCH COPYRIGHT 2001 ISI (R)
1999:348947 The Genuine Article (R) Number: 182AQ. Randomized trial of growth and development in term infants fed formulas with or without arachidonic acid (AA) and docosahexaenoic acid (DHA) for 1 yr. Auestad N (Reprint); Hall R T; Blatter M M; Erickson J; Bogle M L; **Burks W A**; Montalto M B; Carroll R E; Fitzgerald K M; Innis S M; Singer L; Qiu W; Jacobs J; Halter R. ABBOTT LABS, ROSS PROD DIV, COLUMBUS, OH; CHILDRENS MERCY HOSP, KANSAS CITY, MO 64108; ARKANSAS CHILDRENS HOSP, LITTLE ROCK, AR 72202; UNIV BRITISH COLUMBIA, VANCOUVER, BC V5Z 1M9, CANADA; RAINBOW BABIES & CHILDRENS HOSP, CLEVELAND, OH 44106. PEDIATRIC RESEARCH (APR 1999) Vol. 45, No. 4, Part 2, pp. 1627-1627. Publisher: INT PEDIATRIC RESEARCH FOUNDATION, INC. 351 WEST CAMDEN ST, BALTIMORE, MD 21201-2436. ISSN: 0031-3998. Pub. country: USA; CANADA. Language: English.

L2 ANSWER 12 OF 50 MEDLINE DUPLICATE 10
2000428679 Document Number: 20031792. PubMed ID: 10563909. Preparation and functional properties of rice bran protein isolate. Wang M; Hettiarachchy N S; Qi M; **Burks W**; Siebenmorgen T. (Department of Food Science, University of Arkansas, Fayetteville, 72703, USA.) JOURNAL

OF AGRICULTURAL AND FOOD CHEMISTRY, (1999 Feb) 47 (2) 411-6. Journal code: H3N; 0374755. ISSN: 0021-8561. Pub. country: United States. Language: English.

AB Rice bran protein isolate (RBPI) containing approximately 92.0% protein was prepared from unstabilized and defatted rice bran using phytase and xylanase. The yield of RBPI increased from 34% to 74.6% through the use of the enzymatic treatment. Nitrogen solubilities of RBPI were 53, 8, 62, 78, 82, and 80% at pHs 2.0, 4.0, 6.0, 8.0, 10.0, and 12.0, respectively. Differential scanning calorimetry showed that RBPI had denaturation temperature of 83.4 degrees C with low endotherm (0.96 J/g of protein). RBPI had similar foaming properties in comparison to egg white. But emulsifying properties of RBPI were significantly lower than those of bovine serum albumin. The result of amino acid analysis showed that RBPI had a similar profile of essential amino acid requirements for 2-5-year-old children in comparison to that of casein and soy protein isolate.

L2 ANSWER 13 OF 50 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.DUPLICATE 11
1999416915 EMBASE Introduction: Food sensitivity. **Burks W.. W.** Burks, Department of Pediatrics, Univ. of Arkansas for Med. Sciences, Little Rock, AR 72202, United States. Clinical Reviews in Allergy and Immunology 17/3 (277-278) 1999.
Refs: 3.
ISSN: 1080-0549. CODEN: CRVADD. Pub. Country: United States. Language: English.

L2 ANSWER 14 OF 50 BIOSIS COPYRIGHT 2001 BIOSIS
1999:269878 Document No.: PREV199900269878. Randomized trial of growth and development in term infants fed formulas with or without arachidonic acid (AA) and docosahexaenoic acid (DHA) for 1 yr. Auestad, N. (1); Hall, R. T.; Blatter, Mark M.; Erickson, J.; Bogle, M. L.; **Burks, W. A.**; Montalto, Michael B.; Carroll, R. E.; Fitzgerald, K. M.; Innis, Sheila M.; Singer, L.; Qiu, W.; Jacobs, J.; Halter, R.. (1) Ross Products Division, Abbott Laboratories, Columbus, OH USA. Pediatric Research, (April, 1999) Vol. 45, No. 4 PART 2, pp. 276A. Meeting Info.: Annual Meeting of the American Pediatric Society and the Society for Pediatric Research San Francisco, California, USA May 1-4, 1999 ISSN: 0031-3998. Language: English.

L2 ANSWER 15 OF 50 MEDLINE DUPLICATE 12
1999367825 Document Number: 99367825. PubMed ID: 10436387.
Peanut-induced anaphylactic reactions. **Burks W**; Bannon G A; Sicherer S; Sampson H A. (Division of Pediatric Allergy and Immunology, Department of Pediatrics, University of Arkansas for Medical Sciences, Arkansas Children's Hospital, Little Rock, USA.) INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY, (1999 Jul) 119 (3) 165-72. Ref: 43. Journal code: BJ7; 9211652. ISSN: 1018-2438. Pub. country: Switzerland. Language: English.

AB Food allergies, particularly to peanuts, are a common cause of anaphylaxis. Approximately 125 people die each year in the USA secondary to food-induced anaphylaxis. Clinical anaphylaxis is a syndrome of diverse etiology and dramatic presentation of symptoms associated with the classic features of type I, IgE-mediated hypersensitivity [1]. Typically the term anaphylaxis connotes an immunologically-mediated event that occurs after exposure to certain foreign substances. This reaction results from the generation and release of a variety of potent biologically active mediators and their concerted effects on various target organs.

Anaphylaxis is recognized by cutaneous, respiratory, cardiovascular, and gastrointestinal signs and symptoms occurring singly or in combination. This article focuses on allergic reactions to peanuts that manifest as signs and symptoms involving multiple target organs or the cardiovascular system alone.

L2 ANSWER 16 OF 50 SCISEARCH COPYRIGHT 2001 ISI (R)
1998:176816 The Genuine Article (R) Number: YW339. Characterization of beef-specific IgE reactivities and crossreacting allergens.. Ayuso R (Reprint); Reese G; Ibanez M D; Esteban M M; **Burks W A**; Sussman G; Owenby D W; Schwartz H; Lopez M; Lehrer S B. TULANE UNIV, MED CTR, NEW ORLEANS, LA 70118. JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY (JAN 1998) Vol. 101, No. 1, Part 2, pp. 990-990. Publisher: MOSBY-YEAR BOOK INC. 11830 WESTLINE INDUSTRIAL DR, ST LOUIS, MO 63146-3318. ISSN: 0091-6749. Pub. country: USA. Language: English.

L2 ANSWER 17 OF 50 MEDLINE DUPLICATE 13
1998387675 Document Number: 98387675. PubMed ID: 9722220. Peanut allergens. **Burks W**; Sampson H A; Bannon G A. (Department of Pediatrics, University of Arkansas for Medical Sciences and Arkansas Children's Hospital, USA.) ALLERGY, (1998 Aug) 53 (8) 725-30. Ref: 33. Journal code: 39C; 7804028. ISSN: 0105-4538. Pub. country: Denmark. Language: English.

L2 ANSWER 18 OF 50 BIOSIS COPYRIGHT 2001 BIOSIS
1998:154697 Document No.: PREV199800154697. Characterization of beef-specific IgE reactivities and cross-reacting allergens. Ayuso, R.; Reese, G.; Ibanez, M. D.; Esteban, M. Martin; **Burks, W. A.**; Sussman, G.; Owenby, D. W.; Schwartz, H.; Lopez, M.; Lehrer, S. B.. Tulane Univ. Med. Center, New Orleans, LA USA. Journal of Allergy and Clinical Immunology, (Jan., 1998) Vol. 101, No. 1 PART 2, pp. S239. Meeting Info.: 54th Annual Meeting of the American Academy of Allergy, Asthma and Immunology Washington, DC, USA March 13-18, 1998 American Academy of Allergy, Asthma, and Immunology. ISSN: 0091-6749. Language: English.

L2 ANSWER 19 OF 50 SCISEARCH COPYRIGHT 2001 ISI (R)
1998:678973 The Genuine Article (R) Number: 107WX. Implication of Maillard reaction in peanut allergenicity.. Chung S Y (Reprint); Champagne E T; **Burks W A**; Bannon G A. USDA ARS, SO REG RES CTR, NEW ORLEANS, LA 70179; UNIV ARKANSAS MED SCI, LITTLE ROCK, AR 72202. ABSTRACTS OF PAPERS OF THE AMERICAN CHEMICAL SOCIETY (23 AUG 1998) Vol. 216, Part 1, pp. 83-AGFD. Publisher: AMER CHEMICAL SOC. 1155 16TH ST, NW, WASHINGTON, DC 20036. ISSN: 0065-7727. Pub. country: USA. Language: English.

L2 ANSWER 20 OF 50 CAPLUS COPYRIGHT 2001 ACS
1998:530068 Implication of Maillard reaction in peanut allergenicity.. Chung, Si-Yin; Champagne, Elaine T.; **Burks, Wesley A.**; Bannon, Gary A. (ARS, SRRC, USDA, New Orleans, LA, 70179, USA). Book of Abstracts, 216th ACS National Meeting, Boston, August 23-27, AGFD-083. American Chemical Society: Washington, D. C. (English) 1998. CODEN: 66KYA2.
AB It is well known that peanuts contain proteins that are allergenic. However, it is not clear whether after peanut roasting, these proteins would change with respect to their allergenicity. During heating, proteins may react with sugars to form Maillard reaction products which may or may not enhance allergenicity. To det. if such reaction plays a role in peanut allergenicity, a model system involving purified peanut lectin and sugars, such as fructose and ribose, was applied. In the model system, lectin was incubated with fructose, ribose, or no sugar in a buffer soln. (pH 7.4) at 37 .degree.C for 240 h. The resultant lectin adducts were then analyzed in immunoblots for their reactivity toward IgE

antibodies from the serum of a patient with peanut anaphylaxis. Results showed that reactions of peanut lectin with fructose and ribose, resp., resulted in the formation of several protein adducts with mol. wts. higher than that of lectin with one exception. While peanut lectin itself was shown to have little reactivity toward IgE, the protein adducts that formed in the Maillard reaction were recognized by IgE antibodies. This suggests that Maillard reaction may have a role in peanut allergenicity, and that through this reaction, proteins may be modified to become allergenic.

L2 ANSWER 21 OF 50 SCISEARCH COPYRIGHT 2001 ISI (R) DUPLICATE 14
1998:141959 The Genuine Article (R) Number: YU124. Surveying Arkansas physicians: Design issues and insights.. Lensing S Y (Reprint); Gillaspy S R; Smith J M; James J R; **Burks W A**. UNIV ARKANSAS MED SCI, ARKANSAS CHILDRENS HOSP, DEPT PEDIAT, LITTLE ROCK, AR 72205. JOURNAL OF INVESTIGATIVE MEDICINE (JAN 1998) Vol. 46, No. 1, pp. A4-A4. Publisher: SLACK INC. 6900 GROVE RD, THOROFARE, NJ 08086. ISSN: 1081-5589. Pub. country: USA. Language: English.

L2 ANSWER 22 OF 50 BIOSIS COPYRIGHT 2001 BIOSIS
1998:421607 Document No.: PREV199800421607. Implication of maillard reaction in peanut allergenicity. Chung, Si-Ying (1); Champagne, Elaine T. (1); **Burks, Wesley A.**; Bannon, Gary A.. (1) USDA, ARS, SRRC, P.O. Box 19687, New Orleans, LA 70179 USA. Abstracts of Papers American Chemical Society, (1998) Vol. 216, No. 1-3, pp. AGFD 83. Meeting Info.: 216th National Meeting of the American Chemical Society Boston, Massachusetts, USA August 23-27, 1998 American Chemical Society. ISSN: 0065-7727. Language: English.

L2 ANSWER 23 OF 50 MEDLINE
1998043841 Document Number: 98043841. PubMed ID: 9384208. Re: "Outbreaks in highly vaccinated populations: implications for studies of vaccine performance". Prevots D R; Watson J C; Redd S C; Atkinson W A; **Burks-Weathers L**; Snyder S; Wainscott B; Finger R. AMERICAN JOURNAL OF EPIDEMIOLOGY, (1997 Nov 15) 146 (10) 881-2. Journal code: 3H3; 7910653. ISSN: 0002-9262. Pub. country: United States. Language: English.

L2 ANSWER 24 OF 50 MEDLINE DUPLICATE 15
97202255 Document Number: 97202255. PubMed ID: 9049782. Multicenter crossover comparison of the safety and efficacy of Intraglobin-F with Gamimune-N, Sandoglobulin, and Gammagard in patients with primary immunodeficiency diseases. Schiff R I; Williams L W; Nelson R P; Buckley R H; **Burks W**; Good R A. (Duke University Medical Center, Durham, North Carolina, USA.) JOURNAL OF CLINICAL IMMUNOLOGY, (1997 Jan) 17 (1) 21-8. Journal code: HRC; 8102137. ISSN: 0271-9142. Pub. country: United States. Language: English.

AB The safety and clinical efficacy of a liquid, beta-propiolactone-stabilized intravenous gamma-globulin, Intraglobin-F, was evaluated in a multicenter, double-blind study comparing Intraglobin-F to Gamimune-N, Sandoglobulin, or Gammagard. beta-Propiolactone stabilizes the IgG molecule to decrease aggregate formation and is a potent virucidal agent that reduces the risk of viral transmission by intravenous gamma-globulin (IVIG) preparations. Twenty-seven patients with primary immunodeficiency diseases were enrolled at three centers. Each patient received 6 months of therapy with either Intraglobin-F or the IVIG preparation that they had received during the preceding 3 months, then crossed over to the other preparation. Twenty-three patients completed the study. One patient withdrew because of an adverse event, generalized urticaria. A second patient withdrew because of fatigue and perceived decreased efficacy.

Adverse reactions were comparable and occurred in 8.7% of the infusions of Intraglobin-F and 6% of the infusions with Sandoglobulin. None were severe or life-threatening. There was no discernible difference in efficacy between any of the products. The number of days when patients noted symptoms in their diaries was similar for Intraglobin-F and the comparison preparations, 4158 vs 4143. Similarly, there were no differences in the number of physician visits (33 vs 22), days missed from work or school (405 vs 404), days with fever (41 vs 47), or days of prophylactic antibiotics (675 vs 642). There was an increase in the number of days when antibiotics were given therapeutically (578 vs 451); most of the difference was attributable to one patient. There also was a difference in the number of days of hospitalization (21 vs 0), but 19 of the days were accounted for by two patients. When the patients were asked to score their feeling of well-being on a scale of 1 to 5, with 1 being entirely well, the mean score for the patients on Intraglobin-F was 1.86 (range, 1.0 to 3.0), compared to 1.85 (range, 1.0 to 3.2) for patients while on the comparison preparations. Trough IgG levels were slightly lower during the period when patients were treated with Intraglobin-F compared to the other products. There were no abnormalities in blood chemistries or hematologic parameters. Thus, Intraglobin-F is comparable to three of the marketed IVIG preparations in efficacy and safety, as well as patient acceptability, and offers the additional benefit of an extra virucidal step to reduce further the risk of transmitting viral infections.

L2 ANSWER 25 OF 50 SCISEARCH COPYRIGHT 2001 ISI (R)
96:770187 The Genuine Article (R) Number: VM665. ABSENCE OF MODIFICATION OF ENDOGENOUS SOY ALLERGENS - REPLY. **BURKS W (Reprint)**; FUCHS R. UNIV ARKANSAS MED SCI HOSP, ARKANSAS CHILDRENS HOSP, DEPT PEDIAT, 1120 MARSHALL ST, LITTLE ROCK, AR, 72202 (Reprint). JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY (OCT 1996) Vol. 98, No. 4, pp. 855. ISSN: 0091-6749. Pub. country: USA. Language: ENGLISH.

L2 ANSWER 26 OF 50 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
96326238 EMBASE Document No.: 1996326238. Absence of modification of endogenous soy allergens [3]. Moneret-Vautrin D.A.; Kanny G.; **Burks W.**; Fuchs R.. Centre Hospitalier Universitaire, Hopital Central - 29, Ave. Marechal de Lattre de Tassigny,54035 Nancy Cedex, France. Journal of Allergy and Clinical Immunology 98/4 (854-855) 1996. ISSN: 0091-6749. CODEN: JACIBY. Pub. Country: United States. Language: English.

L2 ANSWER 27 OF 50 MEDLINE DUPLICATE 16
96316933 Document Number: 96316933. PubMed ID: 8765832. Isolation and characterization of a clone encoding a major allergen (Bla g Bd90K) involved in IgE-mediated cockroach hypersensitivity. Helm R; Cockrell G; Stanley J S; Brenner R J; **Burks W**; Bannon G A. (Department of Pediatrics, University of Arkansas for Medical Sciences, Little Rock 72202, USA.) JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, (1996 Jul) 98 (1) 172-80. Journal code: H53; 1275002. ISSN: 0091-6749. Pub. country: United States. Language: English.
AB Previous studies have established that atopic individuals living in cockroach-infested housing become sensitized to cockroach aeroallergens and produce IgE antibodies to a variety of proteins. We describe the isolation of a complementary DNA clone from an expression library, constructed with messenger RNA from German (Blattella germanica) cockroaches, which encodes a major allergen involved in mediating

cockroach hypersensitivity. Approximately 0.2% of the clones from a lambda ZAP XR cDNA library bound IgE from a patient with cockroach sensitivity. A randomly selected subset of these clones revealed that they were either different isolates of the same gene or members of a closely related gene family. One of the largest clones (a 4 kb insert) from this subset, Bla g Bd90K hybridized to a single mRNA of approximately the same size. DNA sequence analysis showed that this gene consisted of seven 576 bp tandem repeats with a short unique region at either end. No significant sequence homologies were found between the cockroach clone and any other gene reported in the GenBank database. Serum from 17 of 22 (77%) patients with cockroach hypersensitivity identified IgE-binding recombinant protein expressed from clone Bla g Bd90K in Escherichia coli XL-Blue cells as determined by sodium dodecylsulfate-polyacrylamide gel electrophoresis/immunoblot analysis. This recombinant protein migrates with a molecular weight (90 kd) apparently similar to one identified in whole body extracts. We have identified and isolated a cDNA that encodes a major cockroach allergen (Bla g Bd90K) present in German cockroaches.

L2 ANSWER 28 OF 50 MEDLINE DUPLICATE 17
95199032 Document Number: 95199032. PubMed ID: 7891989. Results of Mullerotomy and levator aponeurosis transposition for the correction of upper eyelid retraction in Graves disease. Ceisler E J; Bilyk J R; Rubin P A; **Burks W R**; Shore J W. (Department of Ophthalmology, Eye Plastics and Orbit Service, Massachusetts Eye and Ear Infirmary, Boston.)
OPHTHALMOLOGY, (1995 Mar) 102 (3) 483-92. Journal code: OI5; 7802443. ISSN: 0161-6420. Pub. country: United States. Language: English.
AB BACKGROUND: Upper eyelid retraction in Graves disease may cause functional morbidity and aesthetic deformity. Surgery to correct thyroid-related upper eyelid retraction may result in temporal undercorrection with failure to eliminate lateral eyelid retraction, leading in turn to a poor eyelid contour postoperatively. METHODS: In 1984, one of the authors developed a new procedure for correcting moderate to severe upper eyelid retraction associated with Graves disease. The surgical technique consists of a Mullerotomy and recession of the levator aponeurosis combined with medial transposition of the lateral horn of the levator aponeurosis. The procedure was performed on 37 patients (72 eyelids). Muller's muscle was used as the spacer to set the eyelid height. Transposition of the levator aponeurosis allowed adjustment of eyelid contour. RESULTS: Thirty patients (58 eyelids) had excellent results, six (13 eyelids) had good results, and one (1 eyelid) had a poor result. No patient required re-operation for asymmetry, unacceptable contour, or malposition. Only one eyelid had significant overcorrection, and only one eyelid had significant undercorrection, requiring further surgery. The most frequent unwanted effects were high eyelid crease (24 eyelids) and residual temporal flare (6 eyelids); however, most of these were seen early in the series before the lateral levator transposition modification was added. CONCLUSION: This procedure allows successful and simultaneous correction of both eyelid position and contour in patients with moderate to severe thyroid-related upper eyelid retraction.

L2 ANSWER 29 OF 50 MEDLINE DUPLICATE 18
95337842 Document Number: 95337842. PubMed ID: 7613216. Isolation and characterization of clones encoding cockroach allergens. Helm R; Crespo J

F; Cockrell G; Stanley J S; Brenner R J; **Burks W**; Bannon G A. (Department of Pediatrics, University of Arkansas for Medical Sciences, Little Rock, USA.) INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY, (1995 May-Jun) 107 (1-3) 462-3. Journal code: BJ7; 9211652. ISSN: 1018-2438. Pub. country: Switzerland. Language: English.

L2 ANSWER 30 OF 50 MEDLINE DUPLICATE 19
93357681 Document Number: 93357681. PubMed ID: 8353458. Identification of
cockroach aeroallergens from living cultures of German or American cockroaches. Helm R M; **Burks W**; Williams L W; Milne D E; Brenner R J. (Department of Pediatrics, University of Arkansas for Medical Sciences, Little Rock.) INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY,
(1993) 101 (4) 359-63. Journal code: BJ7; 9211652. ISSN: 1018-2438. Pub. country: Switzerland. Language: English.
AB The Air Sentinel and polytetrafluoroethylene (PTFE) membranes were used to
capture airborne particles over living colonies of German or American cockroaches. Silver-stained SDS-PAGE gels revealed protein bands at 80, 55, 36, and several bands below the 33-kD marker. SDS-PAGE/immunoblots of PTFE eluates from German cockroach colonies incubated with serum from cockroach-sensitive individuals revealed IgE-binding bands with apparent molecular weights of 36 and 80 kD. Only the 36-kD allergen and allergens below the 33-kD marker were evident in the American PTFE eluate. ELISA analysis with a monoclonal antibody assay identified the presence of both Bla g I and Bla g II in the German PTFE eluate. No Bla g I or Bla g II could be identified in the American PTFE eluate. These studies demonstrate
that in addition to Bla g I and Bla g II, several other aerosolized allergens become airborne over cockroach colonies and may be important in the environment where cockroaches are abundant.

L2 ANSWER 31 OF 50 SCISEARCH COPYRIGHT 2001 ISI (R)
92:207210 The Genuine Article (R) Number: HK161. WANTED - CORPORATIONS THAT CARE ABOUT HIGH-SCHOOL SCIENCE STUDENTS - FOR THE CHEMATHON EXPERIENCE. SINGLETON M (Reprint); **BURKS W**; HENRY N; HAAS J; YAMAGUCHI E; WILSON D; MATIS H; DAIRIKI J; KAHN B. ABSTRACTS OF PAPERS OF THE AMERICAN CHEMICAL SOCIETY (05 APR 1992) Vol. 203, Part 1, pp. 350-CHED. ISSN: 0740-0667. Language: ENGLISH.

L2 ANSWER 32 OF 50 MEDLINE
93177161 Document Number: 93177161. PubMed ID: 1290883. Mock hospital ethics committee: the role of ethics committees in resource distribution. Roundtable discussion. Bergen S S Jr; **Burks W**; Nadler G; Olick R; Pickens R; Spiro H. TRENDS IN HEALTH CARE, LAW AND ETHICS, (1992 Spring-Summer) 7 (3-4) 50-6. Journal code: BG3; 9206683. ISSN: 1062-5364.
Pub. country: United States. Language: English.

L2 ANSWER 33 OF 50 MEDLINE DUPLICATE 20
94121029 Document Number: 94121029. PubMed ID: 1688295.
Trimethoprim-sulfamethoxazole oral desensitization in hemophiliacs infected with human immunodeficiency virus with a history of hypersensitivity reactions. Kletzel M; Beck S; Elser J; Shock N; **Burks W**. (Department of Pediatrics, University of Arkansas for Medical Science, Little Rock.) AMERICAN JOURNAL OF DISEASES OF CHILDREN, (1991 Dec) 145 (12) 1428-9. Journal code: 3GS; 0370471. ISSN: 0002-922X.
Pub. country: United States. Language: English.
AB Hemophiliacs infected with human immunodeficiency virus with a history of hypersensitivity reaction to a combination product of trimethoprim and sulfamethoxazole were desensitized orally. Six of the seven patients included in the study successfully completed the desensitization protocol

and received trimethoprim-sulfamethoxazole for 5 to 7 months after desensitization (mean length of treatment, 5.7 months) for prophylaxis of Pneumocystis carinii pneumonia. The small number of patients and the short
follow-up allow us to suggest that oral desensitization may be an effective and inexpensive means to treat hemophiliacs infected with human immunodeficiency virus with trimethoprim-sulfamethoxazole as prophylaxis against Pneumocystis carinii pneumonia.

L2 ANSWER 34 OF 50 SCISEARCH COPYRIGHT 2001 ISI (R) DUPLICATE 21
90:687227 The Genuine Article (R) Number: EN539. ALTERATIONS IN BRAIN-CELLS DURING GVHD. BECK S A (Reprint); **BURKS W**; GRIFFIN S T. UNIV ARKANSAS MED SCI HOSP, LITTLE ROCK, AR, 72205; ARKANSAS CHILDRENS HOSP, LITTLE ROCK, AR, 72202. CLINICAL RESEARCH (1990) Vol. 38, No. 4, pp. A950.
Pub. country: USA. Language: ENGLISH.

L2 ANSWER 35 OF 50 SCISEARCH COPYRIGHT 2001 ISI (R) DUPLICATE 22
90:13838 The Genuine Article (R) Number: CF636. PROPHYLAXIS WITH IMMUNE GLOBULIN IN PEDIATRIC RENAL-TRANSPLANT PATIENTS. ELLIS E N (Reprint); AUGUSTINE A; **BURKS W**; KLETZEL M. UNIV ARKANSAS, LITTLE ROCK, AR, 72204. CLINICAL RESEARCH (1990) Vol. 38, No. 1, pp. A68. Pub. country: USA
. Language: ENGLISH.

L2 ANSWER 36 OF 50 SCISEARCH COPYRIGHT 2001 ISI (R) DUPLICATE 23
90:183726 The Genuine Article (R) Number: CW362. ALTERATIONS IN BRAIN-CELLS DURING GVHD. BECK S A (Reprint); **BURKS W**; GRIFFIN S T. UNIV ARKANSAS MED SCI HOSP, LITTLE ROCK, AR, 72205; ARKANSAS CHILDRENS HOSP, DEPT PEDIAT, LITTLE ROCK, AR, 72202. PEDIATRIC RESEARCH (1990) Vol. 27, No. 4, pp. A38. Pub. country: USA. Language: ENGLISH.

L2 ANSWER 37 OF 50 SCISEARCH COPYRIGHT 2001 ISI (R) DUPLICATE 24
88:597040 The Genuine Article (R) Number: Q6140. NOVEL SYNTHESIS OF 3-FLUORO-1-AMINOADAMANTANE AND SOME OF ITS DERIVATIVES. ANDERSON G L (Reprint); **BURKS W A**; HARRUNA I I. MORRIS BROWN COLL, DEPT CHEM, ATLANTA, GA, 30314 (Reprint). SYNTHETIC COMMUNICATIONS (1988) Vol. 18, No.
16-1, pp. 1967-1974. Pub. country: USA. Language: ENGLISH.

L2 ANSWER 38 OF 50 BIOSIS COPYRIGHT 2001 BIOSIS
1988:64418 Document No.: BR34:31114. AUTOSOMAL DOMINANT TRANSMISSION OF DIGEORGE MALFORMATION COMPLEX. KEPPEN L; FASULES J; **BURKS W**; MILLER C. UNIV. ARKANSAS MED. SCI., LITTLE ROCK, ARKANSAS.. 38TH ANNUAL MEETING OF THE AMERICAN SOCIETY OF HUMAN GENETICS, SAN DIEGO, CALIFORNIA, USA, OCTOBER 7-10, 1987. AM J HUM GENET. (1987) 41 (3 SUPPL), A197. CODEN: AJHGAG. ISSN: 0002-9297. Language: English.

L2 ANSWER 39 OF 50 MEDLINE DUPLICATE 25
86070387 Document Number: 86070387. PubMed ID: 4071146. Ruptured aneurysm
of the internal iliac artery. Boyarsky A H; **Burks W P**; Davidson J T; Chandler J J. SOUTHERN MEDICAL JOURNAL, (1985 Nov) 78 (11) 1356-7. Journal code: UVH; 0404522. ISSN: 0038-4348. Pub. country: United States. Language: English.
AB Our case and others reported in the literature illustrate that isolated aneurysms of the internal iliac artery are uncommon lesions with a highly lethal potential. The classic signs of ruptured abdominal aneurysm--pain, palpable mass, and shock--are usually altered with rupture of these aneurysms because of their deep location in the pelvis. Rectal examination
will aid diagnosis. Surgical management of IIA aneurysms 4 cm or larger is

indicated at the time of diagnosis, since rupture is usually fatal.

L2 ANSWER 40 OF 50 MEDLINE DUPLICATE 26
86066510 Document Number: 86066510. PubMed ID: 2415895. Management of complications following dermis-fat grafting for anophthalmic socket reconstruction. Shore J W; McCord C D Jr; Bergin D J; Dittmar S J; Maiorca J P; **Burks W R.** OPHTHALMOLOGY, (1985 Oct) 92 (10) 1342-50. Journal code: OI5; 7802443. ISSN: 0161-6420. Pub. country: United States. Language: English.

AB Sixty consecutive cases of dermis-fat grafts for anophthalmic socket reconstruction were reviewed to examine the frequency, severity, and management of postoperative complications. In seven patients, the conjunctiva failed to resurface the graft and central ulceration developed. Ten cases resulted in enophthalmos. Two patients developed keratinized sockets with chronic discharge and desquamation. Three patients required excision of conjunctival granulomas. One patient developed a primary graft infection. A donor site hematoma occurred in one patient. Secondary surgical intervention was required in ten patients. Nine complications in eight patients were managed in the office; five complications in four patients were observed and subsequently resolved without surgical intervention. Most complications occurred in patients with severely traumatized sockets who had undergone extensive earlier ocular surgery, or who had a systemic disease contributing to defective wound healing.

L2 ANSWER 41 OF 50 MEDLINE DUPLICATE 27
85277646 Document Number: 85277646. PubMed ID: 4026072. Unsuccessful control of abdominal aortic aneurysm by bypass and ligation. Lipton J S; Tell B L; **Burks W P;** Chandler J J; Davidson J T. AMERICAN SURGEON, (1985 Aug) 51 (8) 460-1. Journal code: 43E; 0370522. ISSN: 0003-1348. Pub. country: United States. Language: English.

AB Two patients developed abdominal aortic aneurysm rupture following bilateral iliac artery ligation and axillobifemoral bypass. The first patient developed his rupture several weeks after outflow ligation and apparent thrombosis of the aneurysm. At autopsy, the aneurysmal rupture occurred in the left posterior junction between the thrombosed aneurysm and the normal aorta. In the second case, the aneurysm was not completely thrombosed and plans were in progress for thrombosis of the aneurysm when the patient developed frank rupture, necessitating operative intervention.

The authors await the published experience of others with bilateral common iliac artery ligation and extra-anatomic bypass for abdominal aortic aneurysm, but these authors do not currently recommend this management plan.

L2 ANSWER 42 OF 50 CAPLUS COPYRIGHT 2001 ACS
1984:571922 Document No. 101:171922 Vinyl chloride monomer. **Burks, William Millard, Jr.** (Stauffer Chemical Co. , USA). Eur. Pat. Appl. EP 111310 A1 19840620, 12 pp. DESIGNATED STATES: R: BE, DE, GB, IT, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1983-112319 19831207. PRIORITY: US 1982-447869 19821208.

AB Ethylene dichloride (I) [107-06-2] is dehydrochlorinated to vinyl chloride [75-01-4] with a large savings in energy in a process involving conducting satd. I vapor to a compressor, compressing from 1 atm to 2 kg/cm2 to 6-14 kg/cm2 gage, and pyrolyzing the compressed vapor. Thus, I at vapor pressure 1.0 kg/cm2 was compressed to 10.0 kg/cm2 gage and 185.degree. using 720,000 kcal/h based on a feed rate of 40,000 kg I/h. A conventional process based on the same feed rate in which I at 40.degree. was taken from a storage tank and preheated and vaporized to 185.degree.

and 10.0 kg/cm2 gage required 4,250,000 kcal/h.

L2 ANSWER 43 OF 50 SCISEARCH COPYRIGHT 2001 ISI (R)
84:535349 The Genuine Article (R) Number: TG059. UNUSUAL COMPLICATIONS FROM AN ORBITAL FLOOR IMPLANT. SHAGETS F W (Reprint); SHORE J W; BIZON J B; **BURKS W R.** OTOLARYNGOLOGY-HEAD AND NECK SURGERY (1984) , pp. 79. Language: ENGLISH.

L2 ANSWER 44 OF 50 CAPLUS COPYRIGHT 2001 ACS
1984:39118 Document No. 100:39118 Treating liquid chlorinated hydrocarbon wastes containing iron. **Burks, William, Jr.**; Doane, Elliott P.; Campbell, Ramsey G.; Velez, Emilio S. (Stauffer Chemical Co. , USA). Eur.
Pat. Appl. EP 94527 A1 19831123, 29 pp. DESIGNATED STATES: R: BE, CH, DE, FR, GB, IT, LI, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1983-104079 19830426. PRIORITY: US 1982-378368 19820514.
AB Plugging of waste heat boilers or fluidized beds for incineration of chlorinated hydrocarbon wastes from vinyl chloride [75-01-4] manuf. (heavy ends) is prevented by dissolving FeCl3 and other metallic contaminants in a dil. mineral acid. Thus, a bottoms stream from a heavy ends column from low temp. C2H4 chlorination was treated with an equal vol. of 1N HCl for 1-2 min. The org. phase FeCl3 concn. decreased from 1 wt.% to .apprx.25-55 ppm.

L2 ANSWER 45 OF 50 MEDLINE
72088985 Document Number: 72088985. PubMed ID: 4500445. A method of cholecystectomy and operative cholangiography. Chandler J J; **Burks W P**; Miller D B. JOURNAL OF THE MEDICAL SOCIETY OF NEW JERSEY, (1972 Jan) 69 (1) 45-9. Journal code: J47; 7503084. ISSN: 0025-7524. Pub. country: United States. Language: English.

L2 ANSWER 46 OF 50 MEDLINE DUPLICATE 28
71115858 Document Number: 71115858. PubMed ID: 5101698. Popliteal artery occlusion by subadventitial pseudocyst: case report and summary of world literature. Chandler J J; **Burks W P.** SURGERY, (1971 Mar) 69 (3) 474-7. Journal code: VC3; 0417347. ISSN: 0039-6060. Pub. country: United States. Language: English.

L2 ANSWER 47 OF 50 MEDLINE
69157175 Document Number: 69157175. PubMed ID: 4975984. The colonic polyp: observation or excision?. Miller D B; Chandler J J; **Burks W P.** CA: A CANCER JOURNAL FOR CLINICIANS, (1969 Mar-Apr) 19 (2) 118-9. Journal code: CB5; 0370647. ISSN: 0007-9235. Pub. country: United States. Language: English.

L2 ANSWER 48 OF 50 MEDLINE
68095055 Document Number: 68095055. PubMed ID: 5235376. The colonic polyp: observation or excision?. Miller D B; Chandler J J; **Burks W P.** JOURNAL OF THE MEDICAL SOCIETY OF NEW JERSEY, (1967 Oct) 64 (10) 549-50. Journal code: J47; 7503084. ISSN: 0025-7524. Pub. country: United
States. Language: English.

L2 ANSWER 49 OF 50 CAPLUS COPYRIGHT 2001 ACS
1964:82443 Document No. 60:82443 Original Reference No. 60:14384f-h Chlorination of methane. **Burks, William M., Jr.**; Obrecht, Robert P. (Stauffer Chemical Co.). US 3126419 19640324, 9 pp. (Unavailable). APPLICATION: US 19600926.
AB The multiple-series reactor used in the partial chlorination of CH4 was operated by feeding Cl, CH4, and CCl4 diluent to a first reactor zone maintained at 350-550.degree.. The gaseous product stream contg. unreacted CH4, HCl, CCl4, and partially chlorinated hydrocarbons, including CHCl3 and CH2Cl2, was cooled (-25.degree.) to condense CCl4,

CHCl3, and CH2Cl2 in the stream. The remaining gaseous material, including all HCl produced, was passed to a second reactor zone, also maintained at the above temp., and addnl. Cl and CCl4 mixed with it to form a gaseous product stream contg. unreacted CH4, HCl, CCl4, and partially chlorinated hydrocarbons, including CHCl3 and CH2Cl2. This was cooled as above to condense CCl4, CHCl3, and CH2Cl2 from the product stream, HCl removed from the remaining portions of the product stream, the remaining gaseous materials dried and recycled through at least one of the reaction zones, and addnl. Cl and diluent, mixed with the gaseous materials, being recycled through the last reaction zone. This multiple reactor system makes possible the redn. of diluent requirements to far more convenient and manageable levels. An advantage also lies in the ability to achieve a product distribution favorable to the higher mol. wt. components without resorting to elaborate auxiliary heat control facilities. Flow sheets are given which show the sequence of steps in the process, the effect of varying the molar ratio of reactants upon certain other variables, diluent requirements at given Cl ratios required for continuous operation at 475.degree. and contrasting such diluent requirements for the multiple series reactor system employing two reactors with intermediate condensation.

L2 ANSWER 50 OF 50 MEDLINE
60104842 Document Number: 60104842. A study of the causes and treatment of external postoperative intestinal fistulas. WEST J P; RING E M; MILLER R E; **BURKS W P**. Suvr Med (Sofiia), (1961 Oct) 113 490-6.
Language: English.

=> s allergen

L3 91388 ALLERGEN

=> s l3 and modified

L4 2043 L3 AND MODIFIED

=> s l4 and IL12

L5 0 L4 AND IL12

=> s l4 and interleukin 12

L6 16 L4 AND INTERLEUKIN 12

=> dup remove l6

PROCESSING COMPLETED FOR L6
L7 12 DUP REMOVE L6 (4 DUPLICATES REMOVED)

=> s l7 and interleukin 16

L8 1 L7 AND INTERLEUKIN 16

=> d l8 cbib abs

L8 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2001 ACS
1999:495393 Document No. 131:143513 Methods and reagents for decreasing

allergic reactions. Sosin, Howard; Bannon, Gary A.; Burks, A. Wesley, Jr.; Sampson, Hugh A. (University of Arkansas, USA; Mt. Sinai School of Medicine of the City University of New York). PCT Int. Appl. WO 9938978 A1 19990805, 46 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US2031 19990129. PRIORITY: US 1998-PV73283 19980131; US 1998-PV74590 19980213; US 1998-PV74624 19980213;
US 1998-PV74633 19980213; US 1998-141220 19980827.

AB It has been detd. that **allergens**, which are characterized by both humoral (IgE) and cellular (T cell) binding sites, can be **modified** to be less allergenic by modifying the IgE binding sites. The IgE binding sites can be converted to non-IgE binding sites by masking the site with a compd. that prevents IgE binding or by altering as little as a single amino acid within the protein, most typically a hydrophobic residue towards the center of the IgE-binding epitope, to eliminate IgE binding. The method allows the protein to be altered as minimally as possible, other than within the IgE-binding sites, while retaining the ability of the protein to activate T cells, and, in some embodiments by not significantly altering or decreasing IgG binding capacity. The examples use peanut **allergens** to demonstrate alteration of IgE binding sites. The crit. amino acids within each of the IgE binding epitopes of the peanut protein that are important to Ig binding have been detd. Substitution of even a single amino acid within each of the epitopes led to loss of IgE binding. Although the epitopes shared no common amino acid sequence motif, the hydrophobic residues located in the center of the epitope appeared to be most crit. to IgE binding.

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=> d his

     (FILE 'HOME' ENTERED AT 09:19:30 ON 06 JUN 2001)

     FILE 'MEDLINE, EMBASE, SCISEARCH, BIOSIS, CAPLUS' ENTERED AT 09:19:45 ON
     06 JUN 2001
L1          113 S BURKS W?/AU
L2           50 DUP REMOVE L1 (63 DUPLICATES REMOVED)
L3        91388 S ALLERGEN
L4         2043 S L3 AND MODIFIED
L5            0 S L4 AND IL12
L6           16 S L4 AND INTERLEUKIN 12
L7           12 DUP REMOVE L6 (4 DUPLICATES REMOVED)
L8            1 S L7 AND INTERLEUKIN 16

=> s l4 and interleukin

L9          156 L4 AND INTERLEUKIN

=> s l9 and IL12

L10           0 L9 AND IL12

=> dup remove l9

PROCESSING COMPLETED FOR L9
L11          75 DUP REMOVE L9 (81 DUPLICATES REMOVED)
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=> s l11 and interleukin 12

L12 11 L11 AND INTERLEUKIN 12

=> dup remove l12

PROCESSING COMPLETED FOR L12
L13 11 DUP REMOVE L12 (0 DUPLICATES REMOVED)

=> d l13 1-11 cbib abs

L13 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2001 ACS
2000:741936 Document No. 133:308997 Methods for skewing the balance between Th1 and Th2 immune responses. Bottomly, H. Kim; Caplan, Michael J.; Sosin, Howard B. (Panacea Pharmaceuticals, LLC, USA). PCT Int. Appl. WO 2000061157 A1 20001019, 76 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU,
AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US9270 20000407.
PRIORITY: US 1999-290029 19990409.
AB The present invention provides compns. and methods for regulating immune system reactions by biasing T cell responses away from Th1 or Th2 responses in a pre-detd. manner. Control is effected at the stage of antigen/APC encounter and/or at the stage of APC/T cell encounter. In preferred embodiments, a Th1 or Th2 response is inhibited through induction of the alternative response. The inventive methods and reagents
are particularly useful for the management of autoimmune disorders, allergy, and asthma.

L13 ANSWER 2 OF 11 MEDLINE
2000429040 Document Number: 20384768. PubMed ID: 10925258. T cell reactivity with allergoids: influence of the type of APC. Kahlert H; Grage-Griebenow E; Stuwe H T; Cromwell O; Fiebig H. (Allergopharma Joachim
Ganzer KG, Reinbek, Germany.. allergopharmakg@csi.com) . JOURNAL OF IMMUNOLOGY, (2000 Aug 15) 165 (4) 1807-15. Journal code: IFB; 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.
AB The use of allergoids for **allergen**-specific immunotherapy has been established for many years. The characteristic features of these chemically **modified allergens** are their strongly reduced IgE binding activity compared with the native form and the retained immunogenicity. T cell reactivity of chemically **modified allergens** is documented in animals, but in humans indirect evidence of reactivity has been concluded from the induction of **allergen**-specific IgG during immunotherapy. Direct evidence of T cell reactivity was obtained recently using isolated human T cells. To obtain further insight into the mechanism of action of allergoids, we compared the Ag-presenting capacity of different APC types, including DC and macrophages, generated from CD14+ precursor cells from the blood of grass pollen allergic subjects, autologous PBMC, and B cells. These APC were used in experiments together with Phl p 5-specific T cell clones under stimulation with grass pollen **allergen** extract, rPhl p 5b, and the respective allergoids. Using DC and macrophages, allergoids exhibited a pronounced and reproducible T cell-stimulating capacity.

Responses were superior to those with PBMC, and isolated B cells failed to present allergoids. Considerable IL-12 production was observed only when using the DC for Ag presentation of both **allergens** and allergoids. The amount of IL-10 in supernatants was dependent on the phenotype of the respective T cell clone. High IL-10 production was associated with suppressed IL-12 production from the DC in most cases. In conclusion, the reactivity of Th cells with allergoids is dependent on the type of the APC.

L13 ANSWER 3 OF 11 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

2001086644 EMBASE [Immunophysiopathology of allergic contact dermatitis]. IMMUNOFISIOPATOLOGIA DELLA DERMATITE ALLERGICA DA CONTATTO. Valsecchi R.. R. Valsecchi, Clinica Dermatologica, Ospedali Riuniti, Largo Barozzi, 1, 24100 Bergamo, Italy. Annali Italiani di Dermatologia Clinica e Sperimentale 54/3 (135-140) 2000.
Refs: 35.
ISSN: 0365-169X. CODEN: ADCRAG. Pub. Country: Italy. Language: Italian. Summary Language: English; Italian.

AB Allergic contact dermatitis (ACD) is one of the more frequent and frustrating dermatological problems. In recent years much knowledge has been gained in the understanding of ACD, both with respect to basic mechanisms and to clinical aspects. However, despite all the clinical and scientific research, a thorough understanding of the disease remains elusive. ACD results from cell-mediated (type IV) hypersensivity, and this immunologic reaction requires the intervention of four factors: hapten (natural or synthetic substance), epidermal cells (mainly keratinocytes and Langerhans cells which are the first relay stage in the immunological response), CD4+ T-cells which enter into contact with Langerhans cells, and reactivated cells such as monocytes, macrophages, neutrophils etc. ACD develops when the epidermis comes into contact with exogenous substances which, after penetrating the epidermis, trigger the immune response; this response consists of two phases, induction (afferent phase) and elicitation (efferent phase), and subsequently there is a resolution phase. The main events which occur in the ACD afferent limb are consecutively: Conjugation of apten with skin components, recognition of these hapten-**modified** components by specific T-cells, proliferation of specific T-cells in draining lymph nodes and propation of specific T-cells progens over the body. The efferent limb of the cellular immune response is based on the increased frequency of T-cells with a given-specificity throughout the body of a sensitized individual, whereas at primary allergenic skin contact too few specific T-cells are locally available to allow for macroscopically detectable skin reactivity. When challenging a sensitized individual a local inflammatory reaction will follow and local interaction will be possible between **allergen** presenting cells and specific T-cells, leading to local lymphokine production within the skin. The release of these mediators, many of which have a pro-inflammatory action, causes the arrival of more T-cells, including specific Tcells that amplify the local mediator release. This leads to a gradually developing eczematous reaction which reaches a maximum after 18 to 48 hr. The lymphokines that play a major role in the development of allergic contact reaction are those with stimulatory effects on the lymphocytes (IL-2, IF-gamma), on mononuclear phagocytes (chemiotactic factor, migration inhibition factor, etc), and on mast cells and vasculature. The resolution phase of ACD is influenced by epidermalderived products, mast cells and basophils. Following antigenic challenge, there is a delayed peak of mast cell degranulation at 48 hr, when the response is typically waning. This suggests that histamine, which

exerts a stimulatory effect on CD8+ T-lymphocytes, may be involved in down regulating the reaction in the later stages; and the basophils may play a similar role in the down regulation of sensitivity. Finally, macrophages and T-cells may also be involved in turning off the immune response. Under stimulation by IF-gamma, macrophages produce prostaglandins especially of E series, and these can inhibit the production of IL-2 and the expression of its specific receptor (IL-2R), and they can also inhibit natural killer cell activation by their inhibition of IL-2.

L13 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2001 ACS

1999:495393 Document No. 131:143513 Methods and reagents for decreasing allergic reactions. Sosin, Howard; Bannon, Gary A.; Burks, A. Wesley, Jr.; Sampson, Hugh A. (University of Arkansas, USA; Mt. Sinai School of Medicine of the City University of New York). PCT Int. Appl. WO 9938978 A1 19990805, 46 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US2031 19990129. PRIORITY: US 1998-PV73283 19980131; US 1998-PV74590 19980213; US 1998-PV74624 19980213; US 1998-PV74633 19980213; US 1998-141220 19980827.

AB It has been detd. that **allergens**, which are characterized by both humoral (IgE) and cellular (T cell) binding sites, can be **modified** to be less allergenic by modifying the IgE binding sites. The IgE binding sites can be converted to non-IgE binding sites by masking the site with a compd. that prevents IgE binding or by altering as little as a single amino acid within the protein, most typically a hydrophobic residue towards the center of the IgE-binding epitope, to eliminate IgE binding. The method allows the protein to be altered as minimally as possible, other than within the IgE-binding sites, while retaining the ability of the protein to activate T cells, and, in some embodiments by not significantly altering or decreasing IgG binding capacity. The examples use peanut **allergens** to demonstrate alteration of IgE binding sites. The crit. amino acids within each of the IgE binding epitopes of the peanut protein that are important to Ig binding have been detd. Substitution of even a single amino acid within each of the epitopes led to loss of IgE binding. Although the epitopes shared no common amino acid sequence motif, the hydrophobic residues located in the center of the epitope appeared to be most crit. to IgE binding.

L13 ANSWER 5 OF 11 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

1999169128 EMBASE **Modified** T-cell activation pattern during specific immunotherapy (SIT) in cat-allergic patients. Meissner N.; Kochs S.; Coutelle J.; Kussebi F.; Baumgarten C.; Lowenstein H.; Kunkel G.; Renz H.. H. Renz, Inst. of Lab. Med./Pathobiochemistry, Charite-Virchow-Klinikum, Humboldt-University, Augustenburger Platz 1, 13353 Berlin, Germany. Clinical and Experimental Allergy 29/5 (618-625) 1999. Refs: 36.
ISSN: 0954-7894. CODEN: CLEAEN. Pub. Country: United Kingdom. Language: English. Summary Language: English.

AB Objective The aim of the study was to analyse early effects of specific immunotherapy (SIT) on immune functions in cat-allergic patients. Methods: Immunological responses of peripheral blood mononuclear cells from eight

cat- allergic patients were analysed before and after SIT in comparison with 11 nonallergic controls. Cells were stimulated in vitro with either bacterial superantigen, mitogen, or cat **allergen**. Production of IL-12 and TH1/TH2 cytokines was analysed by ELISA and lymphocyte subset distribution was assessed by flow-cytometry. Results: We found a significantly reduced secretion of IL-12 (P<0.05) from cells of allergic individuals compared with the controls. This finding was associated with significantly lower IFN-.gamma. production after stimulation with **allergen** (P<0.05) that did not increase during SIT. However, no significant differences were seen after stimulation with mitogen indicating an **allergen** specific IFN-.gamma. secretion response in allergic individuals. Prior to SIT IL-5 production was significantly higher in cells of allergic donors stimulated with **allergen** < 0.005 or mitogen (< 0.05). After reaching the maintenance dose for SIT, **allergen**-induced IL-5 production returned to normal levels, whereas it remained elevated after stimulation with mitogen. These changes were associated with a reduced frequency of CD45 ROT cells following SIT. Conclusion: These results suggest that SIT exerts early effects on **allergen**-specific T-cell responses with selective inhibition of the up-regulated TH2 immune response.

L13 ANSWER 6 OF 11 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

1998294840 EMBASE Comparison between the in vitro cytokine production of mononuclear cells of young asthmatics with and without immunotherapy (IT).

Van Bever H.P.; Vereecke I.F.; Bridts C.H.; De Clerck L.S.; Stevens W.J.. Dr. W.J. Stevens, Immunol. Allergol./Rheumatol. Dept., University of Antwerp, Universiteitsplein 1, B-2610 Antwerpen, Belgium. Clinical and Experimental Allergy 28/8 (943-949) 1998.
Refs: 25.
ISSN: 0954-7894. CODEN: CLEAEN. Pub. Country: United Kingdom. Language: English. Summary Language: English.

AB Background: The underlying mechanisms of immunotherapy (IT) are still unknown but may be related to modifications of cytokine production of T lymphocytes. Objective: In this study we determined the in vitro **allergen**- induced production of IL-2, IL-4, IL-5, IL-12 and IFN.gamma. of peripheral blood mononuclear cells (PBMC) of eight young asthmatics, aged 15 .+-. 2 years, receiving IT (IT group) and of eight comparable asthmatics, aged 13 .+-. 3.5 years, who never received IT (non-IT group). Methods: All patients suffered from perennial asthma and were allergic to house dust mite (HDM). They were selected if they showed a positive stimulation index (SI) of PBMC after in vitro incubation with HDM (i.e. SI>2). Cells were incubated with and without HDM (10 .mu.g/mL) during 24 h, 48 h and 7 days. Cytokines were determined in the supernatant at the three time points and are expressed as median values in pg/mL. Results: In the IT group the secretion of IL-2 was lower compared with the non-IT group after 7 days incubation of PBMC with HDM (0 vs 33.2, P = 0.008). In both groups maximal secretion of IL-2 was observed after 48 h. In the non-IT group a high value of IL-2 persisted after 7 days, whereas in the IT group a significant decline of IL-2 occurred after 7 days. Although IL-4 secretion was low in all subjects, more patients of the non-IT group showed detectable IL-4 in the HDM cultures after 24 h and 48 h, although the difference was not statistically significant (P = 0.08 and P = 0.28, respectively). Furthermore, IL-4 secretion was lower in the HDM cultures after 24 h in the IT group (1.75 vs 4.1, P = 0.011) and 48 h (2.2 vs 4.1, P = 0.035). IL-5 secretion was lower in the HDM cultures after 24 h (12.4 vs 47.6, P = 0.035) and 48 h (26.8 vs 135, P = 0.046) in the IT group than in the non-IT group. After 7 days of incubation with HDM there

was no difference between the groups. There was no difference between both
groups in secretion of IFN.gamma. and IL-12. Conclusions: These results show a difference in vitro cytokine secretion of PBMC of asthmatics receiving IT compared with asthmatics who never received IT. PBMC of patients receiving IT secrete less IL-2 and IL-5 after in vitro incubation
with HDM and show a tendency to secrete less IL-4. The efficacy of IT may be attributed to a **modified** cytokine secretion of PBMC.

L13 ANSWER 7 OF 11 BIOSIS COPYRIGHT 2001 BIOSIS
1998:489934 Document No.: PREV199800489934. Future directions for **allergen** immunotherapy. Platts-Mills, Thomas A. E. (1); Mueller, Geoffrey A.; Wheatley, Lisa M.. (1) UVA Asthma Allergic Dis. Cent., Univ. Virginia Box 225 HSC, Charlottesville, VA 22908 USA. Journal of Allergy and Clinical Immunology, (Sept., 1998) Vol. 102, No. 3, pp. 335-343. ISSN:
0091-6749. Language: English.
AB Over the last 30 years several approaches to modify immunotherapy have been tested, including allergoids, alum precipitation, and most recently peptides. However, none of these have replaced the traditional regimens. Over the same period our scientific understanding of allergic disease has been transformed. Today it is possible to identify and monitor changes occurring during treatment and to target many different aspects of the immune system. Recombinant technology provides a powerful technique both for sequencing proteins and producing **allergens** in commercial quantities. The recombinant proteins can be **modified** by site-directed mutagenesis so as to decrease their reactivity with IgE antibodies while maintaining reactivity with T cells. Knowledge of the tertiary structure of **allergens** will make it simpler to identify and change surface epitopes. A- completely different approach is to use plasmids to introduce the genes for an **allergen**. The strength of this technique is that the plasmid can be designed to control expression and also to influence the cytokine profile of the response or the isotype of antibodies produced. Finally, different adjuvants can be used with proteins to alter the response. These include IL-12, immunostimulatory sequences of DNA, and bacterial proteins such as those used in HibVax. It is now possible to identify the cells that control the immune response to **allergens** and to design treatments that will either downregulate or change the response of T cells. The challenge is to transform this information into an effective treatment for allergic disease.

L13 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2001 ACS
1996:756546 Document No. 126:17804 Human antibodies derived from immunized xenomice. Kucherlapati, Raju; Jakobovits, Aya; Klapholz, Sue; Brenner, Daniel G.; Capon, Daniel J. (Cell Genesys, Inc., USA). PCT Int. Appl. WO 9634096 A1 19961031, 64 pp. DESIGNATED STATES: W: AU, CA, FI, HU, JP, KR, NO, NZ; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1995-US5500 19950428.
AB Antibodies with fully human variable regions against a specific antigen can be prepd. by administering the antigen to a transgenic animal which has been **modified** to produce such antibodies in response to antigenic challenge, but whose endogenous loci have been disabled. Various subsequent manipulations can be performed to obtain either antibodies per se or analogs thereof.

L13 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2001 ACS
1997:2495 Document No. 126:30350 Human antibodies derived from immunized xenomice. Kucherlapati, Raju; Jakobovits, Aya; Klapholz, Sue; Brenner, Daniel G.; Capon, Daniel J. (Cell Genesys, Inc., USA). PCT Int. Appl. WO 9633735 A1 19961031, 69 pp. DESIGNATED STATES: W: AU, CA, HU, JP, KR, NO, NZ; RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,

PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1996-US5928 19960429.
PRIORITY: US 1995-430938 19950427.

AB Fully human antibodies against a specific antigen can be prepd. by administering the antigen to a transgenic animal which has been **modified** to produce such antibodies in response to antigenic challenge, but whose endogenous loci have been disabled. Various subsequent manipulations can be performed to obtain either antibodies per se or analogs thereof. Antibodies or monoclonal antibodies to human **interleukin** 6, tumor necrosis factor .alpha., CD4, L-selectin, gp39, tetanus toxin, PTH-related protein, and **interleukin** 8 were prepd. in xenomice.

L13 ANSWER 10 OF 11 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

97099632 EMBASE Document No.: 1997099632. In vivo direction of CD4 T cells to Th1 and Th2-like patterns of cytokine synthesis. HayGlass K.T.; Wang M.; Gieni R.S.; Ellison C.; Gartner J.. R.S. Gieni, Department of Pediatrics, Stanford University, Stanford, CA, United States. Advances in Experimental Medicine and Biology 409/- (309-316) 1996.
Refs: 39.
ISSN: 0065-2598. CODEN: AEMBAP. Pub. Country: United States. Language: English. Summary Language: English.

AB Factors that influence the initial development, and continued maintenance, of Th1 or Th2-like responses in vivo play a pivotal role in determining immune effector mechanisms and clinical outcome. Here, we review recent developments in this area with particular emphasis on (i) the ability of chemically **modified** exogenous antigens to preferentially activate Th1- dominated responses in vivo and (ii) the role played by NK cells in initial commitment of naive exogenous antigen-specific T cell to Th1 and Th2-like cytokine synthesis. We find that NK cell depletion of naive mice prior to immunization with OVA (which induces balanced Th0 like responses), or a high Mr polymer (that preferentially elicits OVA-specific Th1-dominated responses), fails to influence the development of cytokine or specific antibody responses. The results argue that NK cells do not play an essential role in shaping induction of immune responses to exogenous antigens, the most common class of inhalant **allergen**.

L13 ANSWER 11 OF 11 MEDLINE

97249338 Document Number: 97249338. PubMed ID: 9095224. Regulation of **interleukin-12** signalling during T helper phenotype development. Jacobson N G; Szabo S J; Guler M L; Gorham J D; Murphy K M. (Department of Pathology, Washington University School of Medicine, St. Louis, Missouri 63110, USA.) ADVANCES IN EXPERIMENTAL MEDICINE AND BIOLOGY, (1996) 409 61-73. Ref: 31. Journal code: 2LU; 0121103. ISSN: 0065-2598. Pub. country: United States. Language: English.

AB The experiments described above have allowed us to define the molecular events in IL-12 signalling. Within minutes after IL-12 treatment of responsive cells, Stat1, Stat3, and Stat4 are tyrosine phosphorylated. These molecules form nuclear DNA-binding complexes consisting of homodimeric Stat1 and heterodimeric Stat3-Stat4 complexes. In a murine in vitro phenotype development model, T cells rapidly and selectively lose their capacity to respond to IL-12 upon acquisition of the Th2 phenotype. This hyporesponsiveness is manifested by the inability of IL-12 to induce IFN gamma production in differentiated Th2 cells, as well as the inability of IL-12 to induce the activation of Stat4. Despite the functional defect of IL-12 signalling in Th2 cells, all known components of the IL-12 signal

transduction pathway are present. We speculate that in Th2 cells, the second receptor chain may be absent or one of the other components may be **modified**. Genetic experiments in Balb/c and B10.D2 strains of mice have demonstrated several differences in T helper differentiation in vitro. Stimulation of T cells under neutral conditions results in a bias of Balb/c T cells toward the Th2 extreme and B10 T cells toward the Th1 extreme of cytokine production. Following stimulation under neutral conditions, B10 T cells retain the ability to respond to IL-12 while Balb/c T cells lose IL-12 responsiveness. Mating experiments have demonstrated that the B10 genetic effect is dominant in F1 mice. Analysis of backcrossed animals has suggested that the ability to respond to IL-12 in the secondary stimulation may be controlled by a single dominant B10 gene. The results we describe may have profound implications for allergy. Since allergic responses are largely due to the activation of the Th2 subset of T lymphocytes, a better understanding of T cell phenotype development may reveal multiple targets for therapeutic intervention. First, a better understanding of Th1 phenotype induction in response to IL-12 may allow prevention of in vivo allergic responses using pharmacological tools which bias **allergen**-specific responses to the Th1 subset. Second, a molecular explantation of why Th2 cells fail to reverse phenotype in response to IL-12 may allow treatment of atopic individuals to remove the disease-promoting T lymphocyte compartment. Finally, a better understanding of the basis for genetic differences in murine T helper cell differentiation may allow us to identify a causative genetic element in humans, yielding better diagnostic and therapeutic methods.

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L15  ANSWER 1 OF 2  MEDLINE
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Interleukin 16 and T-cell chemoattractant activity in bronchoalveolar lavage 24 hours after **allergen** challenge in asthma. Krug N; Cruikshank W W; Tschernig T; Erpenbeck V J; Balke K; Hohlfeld J M; Center D M; Fabel H. (Departments of Respiratory Medicine and Functional and Applied Anatomy, Hannover Medical School, Hannover, Germany.. Krug.Norbert@T-online.de) . AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE, (2000 Jul) 162 (1) 105-11. Journal code: BZS; 9421642. ISSN: 1073-449X. Pub. country: United States. Language: English.

AB IL-16 has been shown to be one of the earliest CD4(+) cell chemoattractants present in BAL 4-6 h after antigen challenge but little is known about its persistence and biological activity after 6 h. We determined the concentration of IL-16 using ELISA and the T-cell chemoattractant activity using a **modified** Boyden chamber assay in unconcentrated BAL fluid from 13 patients with mild asthma and 9 nonatopic control subjects at baseline and 24 h after segmental **allergen** or saline challenge. Furthermore, the percentage of IL-16-producing T cells was determined in the different samples of BAL fluid using a flow cytometric intracellular cytokine assay. Although no substantial levels of IL-16 protein were detectable in BAL fluid from control subjects and patients with asthma at baseline and after saline challenge, IL-16 concentrations were significantly elevated in patients with asthma after **allergen** challenge (median, 97 pg/ml; range, 38-362 pg/ml; $p < 0.01$). Furthermore, there was an increased T-cell chemoattractant activity after **allergen** challenge in patients with asthma ($p < 0.01$), which could be blocked by preincubation with anti-IL-16 antibodies and which correlated significantly with the IL-16 protein levels ($R = 0.90$, $p < 0.01$) and with the level of Fas ligand expression on BAL CD4(+) cells ($R = 0.80$, $p < 0.05$). A high percentage (mean 70-90%) of CD4(+) and CD8(+) cells stained positively for IL-16 in both patients with asthma and control subjects without differences after **allergen** or saline challenge. These data demonstrate that the increased chemotactic activity for T cells in patients with asthma is mainly attributable to IL-16. Although T cells by themselves are able to produce IL-16, other cells, such as epithelial cells, have to be considered as further sources for this cytokine in patients with asthma.

L15 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2001 ACS

1999:495393 Document No. 131:143513 Methods and reagents for decreasing allergic reactions. Sosin, Howard; Bannon, Gary A.; Burks, A. Wesley, Jr.; Sampson, Hugh A. (University of Arkansas, USA; Mt. Sinai School of Medicine of the City University of New York). PCT Int. Appl. WO 9938978 A1 19990805, 46 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US2031 19990129. PRIORITY: US 1998-PV73283 19980131; US 1998-PV74590 19980213; US 1998-PV74624 19980213; US 1998-PV74633 19980213; US 1998-141220 19980827.

AB It has been detd. that **allergens**, which are characterized by both humoral (IgE) and cellular (T cell) binding sites, can be **modified** to be less allergenic by modifying the IgE binding sites. The IgE binding sites can be converted to non-IgE binding sites by masking the site with a compd. that prevents IgE binding or by altering as little as a single amino acid within the protein, most typically a hydrophobic residue towards the center of the IgE-binding epitope, to eliminate IgE binding. The method allows the protein to be altered as minimally as possible, other than within the IgE-binding sites, while retaining the ability of the protein to activate T cells, and, in some embodiments by

not significantly altering or decreasing IgG binding capacity. The examples use peanut **allergens** to demonstrate alteration of IgE binding sites. The crit. amino acids within each of the IgE binding epitopes of the peanut protein that are important to Ig binding have been detd. Substitution of even a single amino acid within each of the epitopes led to loss of IgE binding. Although the epitopes shared no common amino acid sequence motif, the hydrophobic residues located in the center of the epitope appeared to be most crit. to IgE binding.

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L17 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2001 ACS
2000:741936 Document No. 133:308997 Methods for skewing the balance between Th1 and Th2 immune responses. Bottomly, H. Kim; Caplan, Michael J.; Sosin, Howard B. (Panacea Pharmaceuticals, LLC, USA). PCT Int. Appl. WO 2000061157 A1 20001019, 76 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US9270 20000407.
PRIORITY: US 1999-290029 19990409.

AB The present invention provides compns. and methods for regulating immune system reactions by biasing T cell responses away from Th1 or Th2 responses in a pre-detd. manner. Control is effected at the stage of

antigen/APC encounter and/or at the stage of APC/T cell encounter. In preferred embodiments, a Th1 or Th2 response is inhibited through induction of the alternative response. The inventive methods and reagents are particularly useful for the management of autoimmune disorders, allergy, and asthma.

L17 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2001 ACS
1999:495393 Document No. 131:143513 Methods and reagents for decreasing allergic reactions. Sosin, Howard; Bannon, Gary A.; Burks, A. Wesley, Jr.; Sampson, Hugh A. (University of Arkansas, USA; Mt. Sinai School of Medicine of the City University of New York). PCT Int. Appl. WO 9938978 A1 19990805, 46 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US2031 19990129. PRIORITY: US 1998-PV73283 19980131; US 1998-PV74590 19980213; US 1998-PV74624 19980213; US 1998-PV74633 19980213; US 1998-141220 19980827.
AB It has been detd. that **allergens**, which are characterized by both humoral (IgE) and cellular (T cell) binding sites, can be **modified** to be less allergenic by modifying the IgE binding sites. The IgE binding sites can be converted to non-IgE binding sites by masking the site with a compd. that prevents IgE binding or by altering as little as a single amino acid within the protein, most typically a hydrophobic residue towards the center of the IgE-binding epitope, to eliminate IgE binding. The method allows the protein to be altered as minimally as possible, other than within the IgE-binding sites, while retaining the ability of the protein to activate T cells, and, in some embodiments by not significantly altering or decreasing IgG binding capacity. The examples use peanut **allergens** to demonstrate alteration of IgE binding sites. The crit. amino acids within each of the IgE binding epitopes of the peanut protein that are important to Ig binding have been detd. Substitution of even a single amino acid within each of the epitopes led to loss of IgE binding. Although the epitopes shared no common amino acid sequence motif, the hydrophobic residues located in the center of the epitope appeared to be most crit. to IgE binding.

=> s interleukin

L18 521476 INTERLEUKIN

=> s l18 and 18

L19 19736 L18 AND 18

=> s l19 and IL18

L20 76 L19 AND IL18

=> dup remove l20

PROCESSING COMPLETED FOR L20
L21 66 DUP REMOVE L20 (10 DUPLICATES REMOVED)

=> s l21 and allergen

L22 0 L21 AND ALLERGEN

=> d l21 cbib abs

L21 ANSWER 1 OF 66 CAPLUS COPYRIGHT 2001 ACS
2001:64158 Document No. 134:130279 Protein and cDNA sequences of a novel Macaca cynomolgus **interleukin 18**, and diagnostic and therapeutic uses thereof. Trinh, Han N.; Taylor, Alexander H. (Smithkline Beecham Corporation, USA; Smithkline Beecham PLC). PCT Int. Appl. WO 2001005973 A1 20010125, 28 pp. DESIGNATED STATES: W: JP; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US16987 20000621. PRIORITY: US 1999-PV140140 19990621; US 2000-597576 20000620.

AB The invention provides protein and cDNA sequences of a novel Macaca cynomolgus **IL18**, and method for producing **IL18** by recombinant techniques. Also disclosed are methods for screening for compds. which either agonize or antagonize Macaca cynomolgus **IL18**. Such compds. are expected to be useful in treatment of human diseases, including, but not limited to: cancer and auto-immune diseases.

=> s l21 and IgE

L23 0 L21 AND IGE

=> d his

(FILE 'HOME' ENTERED AT 09:19:30 ON 06 JUN 2001)

FILE 'MEDLINE, EMBASE, SCISEARCH, BIOSIS, CAPLUS' ENTERED AT 09:19:45 ON 06 JUN 2001

L1 113 S BURKS W?/AU
L2 50 DUP REMOVE L1 (63 DUPLICATES REMOVED)
L3 91388 S ALLERGEN
L4 2043 S L3 AND MODIFIED
L5 0 S L4 AND IL12
L6 16 S L4 AND INTERLEUKIN 12
L7 12 DUP REMOVE L6 (4 DUPLICATES REMOVED)
L8 1 S L7 AND INTERLEUKIN 16
L9 156 S L4 AND INTERLEUKIN
L10 0 S L9 AND IL12
L11 75 DUP REMOVE L9 (81 DUPLICATES REMOVED)
L12 11 S L11 AND INTERLEUKIN 12
L13 11 DUP REMOVE L12 (0 DUPLICATES REMOVED)
L14 2 S L11 AND INTERLEUKIN 16
L15 2 DUP REMOVE L14 (0 DUPLICATES REMOVED)
L16 2 S L11 AND INTERLEUKIN 18
L17 2 DUP REMOVE L16 (0 DUPLICATES REMOVED)
L18 521476 S INTERLEUKIN
L19 19736 S L18 AND 18
L20 76 S L19 AND IL18
L21 66 DUP REMOVE L20 (10 DUPLICATES REMOVED)
L22 0 S L21 AND ALLERGEN
L23 0 S L21 AND IGE

=> s l18 and IL16

L24 29 L18 AND IL16

=> s l24 and IL12

L25 4 L24 AND IL12

=> dup remove l25

PROCESSING COMPLETED FOR L25
L26 2 DUP REMOVE L25 (2 DUPLICATES REMOVED)

=> d l26 1-2 cbib abs

L26 ANSWER 1 OF 2 MEDLINE DUPLICATE 1
2000150066 Document Number: 20150066. PubMed ID: 10684990. Effects of imipenem and cilastatin on human T-lymphocytes derived from acute leukemia
patients with chemotherapy-induced leucopenia: studies of T-lymphocyte responses in the presence of acute myelogenous leukemia (AML) blast accessory cells. Bruserud O. (Division for Hematology, Department of Medicine, Haukeland University Hospital and the University of Bergen, Bergen, Norway.) INTERNATIONAL JOURNAL OF IMMUNOPHARMACOLOGY, (2000 Jan) 22 (1) 69-81. Journal code: GRI; 7904799. ISSN: 0192-0561. Pub. country: ENGLAND: United Kingdom. Language: English.
AB The effects of imipenem and cilastatin on human T-lymphocytes were studied
in vitro. As responder T-cells were used T-lymphocyte clones derived from acute leukemia patients with chemotherapy-induced cytopenia, and the accessory cells were highly enriched acute myelogenous leukemia (AML) blasts. The effects of imipenem and cilastatin on phytohemagglutinin (PHA), anti-CD3 and anti-CD3+anti-CD28 stimulated activation were assayed,
and in addition drug effects on cytokine-dependent proliferation of activated T-lymphocytes were investigated. Imipenem inhibited IL2-dependent proliferation of activated CD4(+) and CD8(+) T-cell clones, and an inhibition was also detected for IL7-, **IL12**-, IL15-, **IL16**- and IL17-dependent clonal proliferation. Imipenem caused a weak inhibition of anti-CD3- and PHA-stimulated T-cell proliferation when using 50 Gy irradiated AML blast accessory cells derived from various patients, whereas no effect was observed for anti-CD3+anti-CD28 stimulated
and allostimulated activation. Imipenem decreased the release of IL4 and Interferon-gamma by T-cell clones stimulated with anti-CD3 and PHA in the presence of native (nonirradiated) AML blasts. The imipenem effects were observed at concentrations corresponding to levels reached in vivo, whereas even high concentrations of cilastatin did not alter T-cell responses. The T-lymphocyte inhibition is probably caused by a direct effect of imipenem on the T-cells.

L26 ANSWER 2 OF 2 BIOSIS COPYRIGHT 2001 BIOSIS
1998:291450 Document No.: PREV199800291450. Expression of cytokines IL10 and **IL12**-17 in human anterior pituitary adenomas. Green, V. L. (1); Speirs, V. (1); Jeffreys, R. V.; Foy, P.; Mathews, B.; Landolt, A. M.; Atkin, S. L. (1). (1) Dep. Med., Univ. Hull, Hull UK. Journal of Endocrinology, (March, 1998) Vol. 156, No. SUPPL., pp. P204. Meeting Info.: 17th Joint Meeting of the British Endocrine Societies Edinburgh, Scotland, UK March 23-25, 1998 British Endocrine Societies. ISSN: 0022-0795. Language: English.

=> d his

(FILE 'HOME' ENTERED AT 09:19:30 ON 06 JUN 2001)

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     FILE 'MEDLINE, EMBASE, SCISEARCH, BIOSIS, CAPLUS' ENTERED AT 09:19:45 ON
     06 JUN 2001
L1          113 S BURKS W?/AU
L2           50 DUP REMOVE L1 (63 DUPLICATES REMOVED)
L3        91388 S ALLERGEN
L4         2043 S L3 AND MODIFIED
L5            0 S L4 AND IL12
L6           16 S L4 AND INTERLEUKIN 12
L7           12 DUP REMOVE L6 (4 DUPLICATES REMOVED)
L8            1 S L7 AND INTERLEUKIN 16
L9          156 S L4 AND INTERLEUKIN
L10           0 S L9 AND IL12
L11          75 DUP REMOVE L9 (81 DUPLICATES REMOVED)
L12          11 S L11 AND INTERLEUKIN 12
L13          11 DUP REMOVE L12 (0 DUPLICATES REMOVED)
L14           2 S L11 AND INTERLEUKIN 16
L15           2 DUP REMOVE L14 (0 DUPLICATES REMOVED)
L16           2 S L11 AND INTERLEUKIN 18
L17           2 DUP REMOVE L16 (0 DUPLICATES REMOVED)
L18      521476 S INTERLEUKIN
L19       19736 S L18 AND 18
L20          76 S L19 AND IL18
L21          66 DUP REMOVE L20 (10 DUPLICATES REMOVED)
L22           0 S L21 AND ALLERGEN
L23           0 S L21 AND IGE
L24          29 S L18 AND IL16
L25           4 S L24 AND IL12
L26           2 DUP REMOVE L25 (2 DUPLICATES REMOVED)

=> s l4 and interferon gamma

L27          99 L4 AND INTERFERON GAMMA

=> dup remove l27

PROCESSING COMPLETED FOR L27
L28           50 DUP REMOVE L27 (49 DUPLICATES REMOVED)

=> s l28 not 1998

L29          49 L28 NOT 1998

=> s l29 and reduce IgE binding

L30           0 L29 AND REDUCE IGE BINDING

=> s l29 IgE binding

MISSING OPERATOR L29 IGE
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s l29 and IgE

L31          30 L29 AND IGE

=> s l31 and decrease binding

L32           0 L31 AND DECREASE BINDING

=> dup remove l31
```

PROCESSING COMPLETED FOR L31
L33 30 DUP REMOVE L31 (0 DUPLICATES REMOVED)

=> d l33 1-30 cbib abs

L33 ANSWER 1 OF 30 BIOSIS COPYRIGHT 2001 BIOSIS
2000:409339 Document No.: PREV200000409339. Modulation of **allergen** -specific immune responses to the major shrimp **allergen**, tropomyosin, by specific targeting to scavenger receptors on macrophages. Rajagopal, Deepa; Ganesh, Kolumam A.; Subba Rao, Pillarisetti V. (1). (1) Vittal Mallaya Scientific Research Foundation, K.R. Road, Bangalore, 560004 India. International Archives of Allergy and Immunology, (April, 2000) Vol. 121, No. 4, pp. 308-316. print. ISSN: 1018-2438. Language: English. Summary Language: English.
AB Background: Tropomyosin from shrimp is the major cross-reacting crustacean food **allergen**. Earlier studies have led to the purification and immunochemical characterization of the major **IgE** binding epitopes of the **allergen**. Maleylated proteins are known to be specifically targeted to scavenger receptors on macrophage. Since antigens processed and presented by macrophages are known to elicit Th1 type of responses and allergic responses are characterized by polarization towards Th2 phenotype, the possibility of modulation of **allergen** -specific immune responses by targeting of tropomyosin to macrophage via scavenger receptor was explored. Methods: The IgG and **IgE** binding potential of the native maleylated form of tropomyosin was carried out by ELISA and immunoblot. The ability of the native and maleylated form of **allergen** to induce in vitro proliferation of splenocytes from BALB/C mice immunized with both forms of **allergen** was tested. The in vitro production of IL-4 and IFN-gamma by splenocytes from mice immunized with the two forms of **allergen** was determined from culture supernatants. The in vivo production of serum IgG1 and IgG2a antibodies following immunization with native and **modified** **allergens** was monitored by ELISA. Results: The maleylated form of tropomyosin was found to have reduced antigenicity and allergenicity as compared to its native counterpart. The **modified** **allergen** was, however, found to elicit a cellular response similar to native tropomyosin in vitro. Analysis of the cytokine profiles showed a modulation from an IL-4-dominant, proallergic, Th2 phenotype to an IFN-gamma-dominant, antiallergic, Th1 phenotype that could also be correlated to a modulation in the in vivo antibody isotype. Conclusion: The results suggest the possible potential for modulating allergic responses in vivo by selective targeting to macrophages.

L33 ANSWER 2 OF 30 BIOSIS COPYRIGHT 2001 BIOSIS
2000:457024 Document No.: PREV200000457024. The involvement of CD80 and CD86 molecules in CD4+ T cell activation in atopic bronchial asthma. Hirata, Hirokuni (1); Arima, Masafumi; Yukawa, Tatsuo; Fukuda, Takeshi. (1) Department of Pulmonary Medicine and Clinical Immunology, Dokkyo University School of Medicine, Mibu, Tochigi, 321-0293 Japan. Dokkyo Journal of Medical Sciences, (March, 2000) Vol. 27, No. 1, pp. 41-48. print. ISSN: 0385-5023. Language: English. Summary Language: English.
AB Background: Recent studies have provided evidence that activation of antigen-specific T cells requires to interaction between CD28 on T cells and its ligands, CD80 and CD86 on antigen presenting cells (APCs). Objective: We examined the effects of CD80 and CD86, which are on the surface of monocytes or B cells, as APCs in PBMCs, on cytokine production

in asthmatic subjects. Methods: All subjects included in this study had mild asthmatic symptoms and positive skin test responses with housedust mite and Dermatophagoides pteronyssinus-**IgE** in sera. Peripheral blood mononucleal cells (PBMCs) were isolated from asthmatic (n=5) and non-atopic control subjects (n=5) and CD4+ T cells were cultured with monocytes or B cells isolated from the PBMCs. PBMCs or CD4+ T cells and either B cells or monocytes were cultured in the presence of anti-CD80 or-CD86 blocking antibodies (Abs) in order to determine cytokine production by CD4+ T cells. To determine production of IL-5 and IFN-gamma, ELISA and FACS analyses were performed on culture supernatants and intracellular cytokines, respectively, after 72h. Results: Our findings clearly showed that **allergen**-induced IL-5 containing CD4+ T cells can be thus **modified** by mixed CD4+ T cells and monocytes, but not by B cells. IL-5 production, but not that of IL-4 or IFN-gamma, cultured with monocytes in stimulation with mite extract, was significantly increased, and significantly suppressed in the presence of anti-CD86 Abs. Inhibition of anti-CD86 mAbs strikingly and anti-CD80 mAbs significantly decreased IL-5 production in PBMCs from asthmatic subjects, but not from non-atopic controls. Conclusion: Our findings suggest that PBMCs in bronchial asthma play an important role in monocytes as APCs, and **allergen**-induced T cell activation and IL-5 production in bronchial asthma subjects is susceptible to blockade by agents interfering with co-stimulation via CD86.

L33 ANSWER 3 OF 30 CAPLUS COPYRIGHT 2001 ACS

1999:495393 Document No. 131:143513 Methods and reagents for decreasing allergic reactions. Sosin, Howard; Bannon, Gary A.; Burks, A. Wesley, Jr.; Sampson, Hugh A. (University of Arkansas, USA; Mt. Sinai School of Medicine of the City University of New York). PCT Int. Appl. WO 9938978 A1 19990805, 46 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US2031 19990129. PRIORITY: US 1998-PV73283 19980131; US 1998-PV74590 19980213; US 1998-PV74624 19980213; US 1998-PV74633 19980213; US 1998-141220 19980827.

AB It has been detd. that **allergens**, which are characterized by both humoral (**IgE**) and cellular (T cell) binding sites, can be **modified** to be less allergenic by modifying the **IgE** binding sites. The **IgE** binding sites can be converted to non-**IgE** binding sites by masking the site with a compd. that prevents **IgE** binding or by altering as little as a single amino acid within the protein, most typically a hydrophobic residue towards the center of the **IgE**-binding epitope, to eliminate **IgE** binding. The method allows the protein to be altered as minimally as possible, other than within the **IgE**-binding sites, while retaining the ability of the protein to activate T cells, and, in some embodiments by not significantly altering or decreasing IgG binding capacity. The examples use peanut **allergens** to demonstrate alteration of **IgE** binding sites. The crit. amino acids within each of the **IgE** binding epitopes of the peanut protein that are important to Ig binding have been detd. Substitution of even a single amino acid within each of the epitopes led to loss of **IgE** binding. Although the epitopes shared no common amino acid sequence motif, the hydrophobic residues located in the center of the epitope appeared to be most crit. to **IgE** binding.

L33 ANSWER 4 OF 30 SCISEARCH COPYRIGHT 2001 ISI (R)
1999:707293 The Genuine Article (R) Number: 235KN. Regulation of T-helper cell responses to inhalant **allergen** during early childhood.
Macaubas C; Sly P D; Burton P; Tiller K; Yabuhara A; Holt B J; Smallacombe T B; Kendall G; Jenmalm M C; Holt P G (Reprint). TVW TELETHON INST CHILD HLTH RES, DIV CELL BIOL, POB 855, PERTH, WA 6872, AUSTRALIA (Reprint); TVW TELETHON INST CHILD HLTH RES, DIV CELL BIOL, PERTH, WA 6872, AUSTRALIA; LINKOPING UNIV HOSP, CLIN RES CTR, S-58185 LINKOPING, SWEDEN. CLINICAL AND EXPERIMENTAL ALLERGY (SEP 1999) Vol. 29, No. 9, pp. 1223-1231. Publisher: BLACKWELL SCIENCE LTD. P O BOX 88, OSNEY MEAD, OXFORD OX2 0NE, OXON, ENGLAND. ISSN: 0954-7894. Pub. country: AUSTRALIA; SWEDEN. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Background Recent evidence suggests that preschool children manifest patterns of **allergen**-specific skin prick test (SPT) reactivity and in vitro T-cell cytokine production which are similar to that of either atopic or nonatopic adults. However, published studies on this age group involve small sample sizes and a restricted number of cytokines, usually in response to polyclonal stimuli.

Objective To elucidate the relationship between in viva and in vitro immune responses to a major inhalant **allergen** house dust mite (HDM) in preschoolers.

Methods Peripheral blood mononuclear cells (PBMCs) from matched groups of HDM-SPT+ and SPT- 6-year-olds (n = 30 and 29, respectively) tested for PBMC responses to HDM, and cytokine production measured at both the protein and mRNA levels. Immunoglobulin (Ig)E and IgG subclass antibody titres were determined in serum. Interrelationships between in vitro and in vivo HDM responses were examined via multivariate analyses.

Results SPT reactivity to HDM was associated with in vitro production by putative T cells of interleukin (IL)-4, IL-5, IL-9, IL-10, IL-13 and low level IFN gamma, and with production in vivo of **IgE** and (all) IgG subclass antibodies; HDM responses in the SPT- group were restricted mainly to IL-10 and IFN gamma and very low levels of IL-4; IL-6 production from non-T-cell sources was common. The cytokine most associated with positive SPT responses was IL-9; SPT weal diameter correlated positively with IL-4, IL-5 and IL-13 and negatively with IL-10.

Conclusion Detailed analysis of cytokine responses in this very young age group have the potential to uncover subtle relationships between in vivo and in vitro **allergen** reactivity which may be less clear in adults, in whom T-cell response patterns are **modified** via chronic stimulation. The present findings which suggest potentially important roles for IL-9 and IL-10 in the early phase of allergic disease, may be one such example.

L33 ANSWER 5 OF 30 BIOSIS COPYRIGHT 2001 BIOSIS
1999:445209 Document No.: PREV199900445209. Assessing the allergenic potential of genetically **modified** foods. Kimber, I. (1). (1) Zeneca Central Toxicology Laboratory, Alderley Park, Macclesfield, Cheshire UK. Human & Experimental Toxicology, (Aug., 1999) Vol. 18, No. 8, pp. 519. Meeting Info.: Annual Congress of the British Toxicology Society Stoke on Trent, England, UK April 18-21, 1999 British Toxicology Society. ISSN: 0960-3271. Language: English.

L33 ANSWER 6 OF 30 CAPLUS COPYRIGHT 2001 ACS
1999:630793 Document No. 132:150780 Pepsin-digested peanut contains T-cell

epitopes but no **IgE** epitopes. Hong, Soo-Jong; Michael, J. Gabriel; Fehringer, Amy; Leung, Donald Y. M. (Division of Allergy-Immunology, The National Jewish Medical and Research, University of Colorado Health Sciences Center, Denver, CO, 80206, USA). J. Allergy Clin. Immunol., 104(2, Pt. 1), 473-477 (English) 1999. CODEN: JACIBY. ISSN: 0091-6749. Publisher: Mosby, Inc..

AB Peanuts are a common cause of food-induced anaphylaxis and fatalities. Previous studies have demonstrated that rush immunotherapy to crude peanut ext. reduces clin. symptoms triggered by oral peanut challenges, but the immunotherapy was assocd. with an unacceptably high incidence of systemic allergic reactions. One approach to reduce the frequency of allergic reactions would be to use a **modified** peanut antigen with low allergenic properties. The authors sought to det. the immunol. characteristics of crude intact peanut ext. before and after pepsin digestion by using **IgE** immunoblotting and assessment of T-lymphocyte responses to intact and peptic digests of peanut exts. Western blot anal. of sera from 5 subjects with peanut allergy showed multiple **IgE**-reactive proteins in crude intact peanut ext. that were eliminated after pepsin treatment of the peanut ext. In contrast, pepsin-digested peanut induced significant T-cell proliferation responses (stimulation index = 30) in vitro in PBMCs from 7 subjects with peanut allergy, albeit at lower levels than that induced by intact peanut (stimulation index = 66). Furthermore, IFN-.gamma. prodn. was induced by intact peanut and pepsin-digested peanut in a concn.-dependent manner. Importantly, T-cell lines generated in response to intact peanut also reacted to pepsin-digested peanut, indicating cross-reactive T-cell epitopes in intact and pepsin-digested peanut. These findings suggest that pepsin-digested peanut may be useful in peanut immunotherapy because pepsin digestion eliminates **IgE** reactivity but maintains T-cell reactivity.

L33 ANSWER 7 OF 30 SCISEARCH COPYRIGHT 2001 ISI (R)

1999:137115 The Genuine Article (R) Number: 165BT. Risk factors for allergy. DeSwert L F A (Reprint). UZ GASTHUISBERG, DEPT PEDIAT, B-3000 LOUVAIN, BELGIUM (Reprint). EUROPEAN JOURNAL OF PEDIATRICS (FEB 1999) Vol. 158, No. 2, pp. 89-94. Publisher: SPRINGER VERLAG. 175 FIFTH AVE, NEW YORK, NY 10010. ISSN: 0340-6199. Pub. country: BELGIUM. Language: English. *ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB Host factors involved in the risk for allergy are heredity, sex, race and age, with heredity being by far the most important. Exposure to **allergens** has been identified as an influential environmental factor, whereas passive smoking and pollution may act as an adjuvant, The atopic mother may - during pregnancy - add to an atopy-prone environment. Whereas respiratory infections are associated with attacks of bronchial asthma, infections in early life might play a role in the protection against atopy by preferential stimulation of a Th1 response, with mutual down-regulation of the Th2 response.

Conclusion Recognition of the risk factors for allergy is important in order to select the factors that could be **modified** for individuals at risk and in order to identify those factors of which the modulation could evolve in general preventive measures.

L33 ANSWER 8 OF 30 SCISEARCH COPYRIGHT 2001 ISI (R)

1999:46577 The Genuine Article (R) Number: 153CM. Responses of human birch pollen **allergen**-reactive T cells to chemically **modified** **allergens** (allergoids). Dormann D; Ebner C; Jarman E R; Montermann E; Kraft D; ReskeKunz A B (Reprint). UNIV MAINZ, KLIN FORSCH GRP ALLERGIE, HAUTKLIN VERFUGUNGSGEBAUDE, DEPT DERMATOL, D-55131 MAINZ, GERMANY (Reprint); UNIV MAINZ, KLIN FORSCH GRP ALLERGIE, HAUTKLIN VERFUGUNGSGEBAUDE, DEPT DERMATOL, D-55131 MAINZ, GERMANY; UNIV VIENNA, INST GEN & EXPT PATHOL, AKH, VIENNA, AUSTRIA. CLINICAL AND EXPERIMENTAL

ALLERGY (NOV 1998) Vol. 28, No. 11, pp. 1374-1383. Publisher: BLACKWELL SCIENCE LTD. P O BOX 88, OSNEY MEAD, OXFORD OX2 0NE, OXON, ENGLAND. ISSN: 0954-7894. Pub. country: GERMANY; AUSTRIA. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Background Allergoids are widely used in specific immunotherapy for the treatment of **IgE**-mediated allergic diseases.

Objective The aim of this study was to analyse whether a modification of birch pollen **allergens** with formaldehyde affects the availability of T-cell epitopes.

Methods Efficient modification of the **allergens** was verified by determining **IgE** and IgG binding activity using ELISA inhibition tests. T-cell responses to birch pollen allergoids were analysed in polyclonal systems, using peripheral blood mononuclear cells (PBMC) of five birch pollen-allergic individuals, as well as birch pollen extract-reactive T-cell lines (TCL), established from the peripheral blood of 14 birch pollen-allergic donors. To determine whether the modification of natural (n)Bet v 1 with formaldehyde or maleic anhydride results in epitope-specific changes in T-cell reactivities, 22 Bet v 1-specific T-cell clones (TCC), established from nine additional birch pollen-allergic individuals, were tested for their reactivity with these products.

Results The majority of PBMC and TCL showed a reduced response to the birch pollen extract allergoid. Bet v 1-specific TCC could be divided into allergoid-reactive and -non-reactive TCC. No simple correlation between possible modification sites of formaldehyde in the respective T-cell epitopes and the stimulatory potential of the allergoid was observed. Mechanisms of suppression or of anergy induction were excluded as an explanation for the non-reactivity of representative TCC. All TCC could be stimulated by maleylated and unmodified nBet v I to a similar extent.

Conclusion These results demonstrate differences in the availability of T-cell epitopes between allergoids and unmodified **allergens**, which are most likely due to structural changes within the **allergen** molecule.

L33 ANSWER 9 OF 30 MEDLINE

1998224476 Document Number: 98224476. PubMed ID: 9564806. Antagonistic peptides specifically inhibit proliferation, cytokine production, CD40L expression, and help for **IgE** synthesis by Der p 1-specific human T-cell clones. Fasler S; Aversa G; de Vries J E; Yssel H. (Human Immunology Department, DNAX Research Institute for Molecular and Cellular Biology, Palo Alto, Calif, USA.) JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, (1998 Apr) 101 (4 Pt 1) 521-30. Journal code: H53; 1275002. ISSN: 0091-6749. Pub. country: United States. Language: English.

AB BACKGROUND: Allergic disorders are characterized by **IgE** antibody responses to a multitude of **allergens** as a result of the ability of these antibodies to specifically bind to high-affinity **IgE** receptors on mast cells and basophils. This interaction results in receptor activation and release of soluble mediators such as histamine and leukotrienes, which cause allergic reactions in various target organs. Because the synthesis of **IgE** is tightly regulated by cytokines and CD40 ligand (L) interactions, CD4+ helper T cells are obvious targets, with the aim to modulate **allergen**-induced **IgE** responses. OBJECTIVES: Because of the central role of **allergen** -specific T-helper type 2 (TH2) cells in the pathway leading to **IgE** synthesis in vitro and in vivo, we have evaluated the possibility of inhibiting **allergen**-induced activation of these

cells by using **allergen**-derived peptides that have been **modified** by single amino acid substitutions. METHODS: Three cloned human TH2-like CD4+ T-cell lines, specific for Der p 1, the major **allergen** in house dust, were used in this study. Upon activation with Der p 1 or specific Der p 1-derived wild-type peptides, these T-cell clones produce high levels of IL-4 and IL-5 and low levels of **interferon-gamma** and IL-2, respectively, and furthermore give help to B cells for the production of **IgE** in vitro. **Modified** synthetic peptides were generated by the introduction of single amino acid substitutions into two different T-cell activation-inducing epitopes on Der p 1. The effects of these **modified** peptides were studied in Der p 1-induced proliferation, cytokine production, and in vitro **IgE** production assays. RESULTS: Several substituted Der p 1-derived peptides failed to induce T-cell proliferation, in contrast to the native peptides. In addition, some of these peptides acted as antagonists by strongly inhibiting wild-type peptide-induced proliferation as well as the production of **interferon-gamma**, IL-2, IL-4, and IL-5, although the production of the latter two cytokines was less affected than that of **interferon-gamma**, even at a 100-fold molar excess of the antagonistic peptides. In addition, the presence of an excess of each of the antagonistic peptides during the activation of Der p I-specific T-cell clones prevented induction of CD40L expression, resulting in a failure of these cells to give help to B cells for the production of **IgE** in vitro, even in the presence of exogenous IL-4. CONCLUSIONS: Substitution of certain amino acid residues in immunogenic Der p 1-derived peptides results in the generation of peptides that fail to induce proliferation of Der p 1-specific T-cell clones. In addition, these **modified** peptides have strong antagonistic activities on Der p 1-induced proliferation, cytokine production, and CD40L expression by **allergen**-specific T-cell clones as well as on T cell-mediated **IgE** production by B cells. These findings suggest that **modified** peptides interfere with **allergen**-induced activation of T cells, including the production of cytokines and the expression of surface molecules important for successful T cell-B cell interactions, and may therefore have therapeutic potential by inhibiting the expansion and function of **allergen**-specific TH2 cells.

L33 ANSWER 10 OF 30 BIOSIS COPYRIGHT 2001 BIOSIS
1998:257635 Document No.: PREV199800257635. Antagonistic peptides specifically inhibit proliferation, cytokine production, CD40L expression, and help for **IgE** synthesis by Der p 1-specific human T-cell clones. Fasler, Stephan; Aversa, Gregoria; De Vries, Jan E.; Yssel, Hans (1). (1) INSERM U454, Hopital Arnaud de Villeneuve, 371 Ave. Doyen Gaston Giraud, 34295 Montpellier Cedex France. Journal of Allergy and Clinical Immunology, (April, 1998) Vol. 10, No. 4 PART 1, pp. 521-530. ISSN: 0091-6749. Language: English.

AB Background: Allergic disorders are characterized by **IgE** antibody responses to a multitude of **allergens** as a result of the ability of these antibodies to specifically bind to high-affinity **IgE** receptors on mast cells and basophils. This interaction results in receptor activation and release of soluble mediators such as histamine and leukotrienes, which cause allergic reactions in various target organs. Because the synthesis of **IgE** is tightly regulated by cytokines and CD40 ligand (L) interactions, CD4+ helper T cells are obvious targets, with the aim to modulate **allergen**-induced **IgE** responses. Objectives: Because of the central role of **allergen**

-specific T-helper type 2 (TH2) cells in the pathway leading to **IgE** synthesis in vitro and in vivo, we have evaluated the possibility of inhibiting **allergen**-induced activation of these cells by using **allergen**-derived peptides that have been **modified** by single amino acid substitutions. Methods: Three cloned human TH2-like CD4+ T-cell lines, specific for Der p 1, the major **allergen** in house dust, were used in this study. Upon activation with Der p 1 or specific Der p 1-dervived wild-type peptides, these T-cell clones produce high levels of IL-4 and IL-5 and low levels of **interferon-gamma** and IL-2, respectively, and furthermore give help to B cells for the production of **IgE** in vitro. **Modified** synthetic peptides were generated by the introduction of single amino acid substitutions into two different T-cell activation-inducing epitopes on Der p 1. The effects of these **modified** peptides were studied in Der p 1-induced proliferation, cytokine production, and in vitro **IgE** production assays. Results: Several substituted Der p 1-derived peptides failed to induce T-cell proliferation, in contrast to the native peptides. In addition, some of these peptides acted as antagonists by strongly inhibiting wild-type peptide-induced proliferation as well as the production of **interferon-gamma**, IL-2, IL-4, and IL-5, although the production of the latter two cytokines was less affected than that of **interferon-gamma**, even at a 100-fold molar excess of the antagonistic peptides. In addition, the presence of an excess of each of the antagonistic peptides during the activation of Der p I-specific T-cell clones prevented induction of CD40L expression, resulting in a failure of these cells to give help to B cells for the production of **IgE** in vitro, even in the presence of exogenous IL-4. Conclusions: Substitution of certain amino acid residues in immunogenic Der p 1-derived peptides results in the generation of peptides that fail to induce proliferation of Der p 1-specific T-cell clones. In addition, these **modified** peptides have strong antagonistic activities on Der p 1-induced proliferation, cytokine production, and CD40L expression by **allergen**-specific T-cell clones as well as on T cell-mediated **IgE** production by B cells. These findings suggest that **modified** peptides interfere with **allergen**-induced activation of T cells, including the production of cytokines and the expression of surface molecules important for successful T cell-B cell interactions, and may therefore have therapeutic potential by inhibiting the expansion and function of **allergen**-specific TH2 cells.

L33 ANSWER 11 OF 30 CAPLUS COPYRIGHT 2001 ACS

1998:726781 Document No. 130:135098 Cytokine secretion patterns of T cells responding to haptenized-human serum albumin in toluene diisocyanate (TDI)-induced asthma patients. Lee, Millina; Park, Sun; Park, Hae-Sim; Youn, Jung Koo (Department of Microbiology, Ajou University School of Medicine, Suwon, 442-749, S. Korea). J. Korean Med. Sci., 13(5), 459-465 (English) 1998. CODEN: JKMSEH. ISSN: 1011-8934. Publisher: Korean Academy of Medical Science.

AB Understanding immune response mechanisms to chem. **allergens** has been limited. It was partly due to the nature of antigens, recognized by T cells, not being well characterized. In the present study, the authors examd. an hypothesis that a reactive chem. **allergen**, toluene diisocyanate (TDI), reacts with autologous proteins, thereby inducing T cell responses to the **modified** self protein in vivo. TDI-human serum albumin (HSA) conjugates were prepd. and the presence of antigenic epitopes on the TDI-HSA conjugate was confirmed by **IgE** ELISA. The authors examd. proliferative and cytokine prodn. responses in TDI-induced asthma patients using the TDI-HSA conjugate as an antigen. Although proliferative responses of peripheral blood mononuclear cells

(PBMCs) were not detected, the prodn. of IFN-.gamma. was obsd. in both PBMC and T cell lines obtained from some newly-diagnosed patients by ELISA. Mitogen-inducible IL-4 prodn. was also detected in some T cell lines. Results of this study may have 2 implications. One is that presentation of haptenized-self protein to the immune system may induce the activation of T cells. The other is that T cells responding to this **modified** self protein may play a role in the pathogenesis of the chem. **allergen**-induced asthma by producing cytokines such as IFN-.gamma. and possibly IL-4.

L33 ANSWER 12 OF 30 SCISEARCH COPYRIGHT 2001 ISI (R)
1998:766648 The Genuine Article (R) Number: 124ZN. Future directions for **allergen** immunotherapy. PlattsMills T A E (Reprint); Mueller G A; Wheatley L M. UNIV VIRGINIA, UVA ASTHMA & ALLERG DIS CTR, BOX 225 HSC, CHARLOTTESVILLE, VA 22908 (Reprint); UNIV VIRGINIA, ASTHMA & ALLERG DIS CTR, CHARLOTTESVILLE, VA 22908. JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY
(SEP 1998) Vol. 102, No. 3, pp. 335-343. Publisher: MOSBY-YEAR BOOK INC.
11830 WESTLINE INDUSTRIAL DR, ST LOUIS, MO 63146-3318. ISSN: 0091-6749.
Pub. country: USA. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Over the last 30 years several approaches to modify immunotherapy have been tested, including allergoids, alum precipitation, and most recently peptides, However, none of these have replaced the traditional regimens. Over the same period our scientific understanding of allergic disease has been transformed. Today it is possible to identify and monitor changes occurring during treatment and to target many different aspects of the immune system. Recombinant technology provides a powerful technique both for sequencing proteins and producing **allergens** in commercial quantities. The recombinant proteins can be **modified** by site-directed mutagenesis so as to decrease their reactivity with **IgE** antibodies while maintaining reactivity with T cells. Knowledge of the tertiary structure of **allergens** will make it simpler to identify and change surface epitopes, A completely different approach is to use plasmids to introduce the genes for an **allergen** . The strength of this technique is that the plasmid can be designed to control expression and also to influence the cytokine profile of the response or the isotype of antibodies produced, Finally, different adjuvants can be used with proteins to alter the response. These include IL-12, immunostimulatory sequences of DNA, and bacterial proteins such as those used in HibVax, It is now possible to identify the cells that control the immune response to **allergens** and to design treatments that will either downregulate or change the response of T cells. The challenge is to transform this information into an effective treatment for allergic disease.

L33 ANSWER 13 OF 30 SCISEARCH COPYRIGHT 2001 ISI (R)
97:381865 The Genuine Article (R) Number: WX987. Anti-IL-4 monoclonal antibody prevents antibiotics-induced active fatal anaphylaxis. Park J S;
Choi I H; Lee D G; Han S S; Ha T Y; Lee J H; Lee W H; Park Y M; Lee H K (Reprint). CHONBUK NATL UNIV, SCH MED, DEPT IMMUNOL, CHONJU 561182, SOUTH KOREA (Reprint); CHONBUK NATL UNIV, SCH MED, DEPT IMMUNOL, CHONJU 561182, SOUTH KOREA; CHONBUK NATL UNIV, SCH MED, DEPT PATHOL, CHONJU 561182, SOUTH
KOREA; CHONBUK NATL UNIV, SCH MED, INST MED SCI, CHONJU 561182, SOUTH KOREA; KOREAN RES INST CHEM TECHNOL, TAEJON, SOUTH KOREA; PUSAN NATL UNIV,
SCH MED, DEPT MICROBIOL, PUSAN 609735, SOUTH KOREA. JOURNAL OF IMMUNOLOGY
(15 MAY 1997) Vol. 158, No. 10, pp. 5002-5006. Publisher: AMER ASSOC IMMUNOLOGISTS. 9650 ROCKVILLE PIKE, BETHESDA, MD 20814. ISSN: 0022-1767.

Pub. country: SOUTH KOREA. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB We previously reported that anti-IL-4 mAb (11B11) failed to prevent protein-induced fatal murine anaphylaxis. To investigate the effect of anti-IL-4 on hapten-induced anaphylaxis, a model of murine anaphylaxis induced by antibiotics, penicillin V (Pen V) and cephalothin (CET), was developed, and the effect of anti-IL-4 on the anaphylaxis was observed. Pen V and CET induced 100 and 70 to 90% fatal reactions, respectively, when C57BL/6 mice were sensitized i.p. with 500 mu g of antibiotic-OVA conjugate with 2 x 10(9) Bordetella pertussis and 1.0 mg of alum and challenged i.v. with 100 mu g of antibiotic-BSA conjugate 14 days later. Serum taken from mice sensitized to Pen V passively sensitized normal mice to develop systemic anaphylaxis, and this ability of the serum was abrogated by heating at 56 degrees C for 2 h or depletion of **IgE**, but not IgG, Abs. Thus, the antibiotic-induced fatal reaction was an **IgE**-dependent anaphylactic reaction. Administration of anti-IL-4 at the beginning of sensitization completely prevented the fatal anaphylactic reactions to both Pen V and CET. This effect of anti-IL-4 was associated with its suppressive activity on antibiotic-specific serum **IgE**, but not IgG, levels. More importantly, anti-IL-4 therapy in previously sensitized mice was also effective in preventing the fatal reactions and rapidly reduced the established **IgE** levels. This study provides a new animal model of hapten-induced anaphylaxis and indicates that blocking of IL-4 activity may be beneficial in allergic diseases caused by a variety of haptens in which **IgE** Abs play a major role.

L33 ANSWER 14 OF 30 SCISEARCH COPYRIGHT 2001 ISI (R)

1998:111115 The Genuine Article (R) Number: YU619. Early effects of rush immunotherapy with Dermatophagoides pteronyssinus in asthmatics. Paranos S (Reprint); Petrovic S. UNIV BELGRADE, MED CTR ZVEZDARA, DEPT ALLERGY CLIN IMMUNOL, D TUCOVICA 161, YU-11000 BELGRADE, YUGOSLAVIA (Reprint). JOURNAL OF INVESTIGATIONAL ALLERGOLOGY & CLINICAL IMMUNOLOGY (NOV-DEC 1997) Vol. 7, No. 6, pp. 588-595. Publisher: J R PROUS SA. APARTADO DE CORREOS 540, PROVENZA 388, 08025 BARCELONA, SPAIN. ISSN: 1018-9068. Pub. country: YUGOSLAVIA. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB In this study we assessed the effects of Dermatophagoides pteronyssinus (Dpt) rush immunotherapy in comparison with placebo treatment in our asthmatic patients. Fourteen highly Dpt-susceptible adults were randomized in two groups (immunotherapy and placebo) and treated in single-blind manner. Patients were selected according to the recommendation of the immunotherapy position paper (1993). To minimize side effects we **modified** the protocol by adjusting **allergen** doses for each patient separately. Immunologic (total and Dpt-specific serum **IgE** and IgG antibodies/EIA, Pharmacia) and clinical parameters (spirometry, medication score and skin testing) were recorded before treatment after 2 weeks, at the second month and after 4 months of immunotherapy onset. None of the patients had life-threatening side effects in the course of the treatment. The results obtained demonstrated significant influence of immunotherapy on Dpt-specific serum IgG synthesis (Kruskal Wallis test $p < 0.05$) and on the late phase skin reaction with Dpt (U-test, $p < 0.05$) at the end of the second month of immunotherapy onset. In the immunotherapy group, we also registered a negative correlation between concentrations of Dpt-specific serum **IgE** and IgG antibodies ($p = -0.83$; $p < 0.05$), at the end of the second month. In

addition, diversities among patients, expressed by immunologic parameters,
were related to the amount of delivered **allergen**. There were no significant differences between groups concerning medication score from opposite to better FEV1, PEFR and dPEFR results (Kruskal Wallis, $p < 0.05$)
in the placebo group. In conclusion, Dpt-specific serum IgG concentration,
immunologic score and late phase skin reactivity to **allergen** appeared to be the valid parameters of rush-immunotherapy achievement, while delivered **allergen** dose also seemed to be an influencing factor.

L33 ANSWER 15 OF 30 MEDLINE
97156828 Document Number: 97156828. PubMed ID: 9003209. Failure of aged rats to accumulate eosinophils in allergic inflammation of the airway. Yagi T; Sato A; Hayakawa H; Ide K. (Second Department of Internal Medicine, Hamamatsu University School of Medicine, Japan.) JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, (1997 Jan) 99 (1 Pt 1) 38-47. Journal code: H53; 1275002. ISSN: 0091-6749. Pub. country: United States. Language: English.
AB To investigate the effect of aging on the allergic airway response, we examined the bronchoconstrictive responses and cellular inflammatory changes in a rat model of bronchial asthma by evaluating young and old animals. Two different age groups of Brown-Norway rats, actively sensitized by injection of ovalbumin into the foot pads, were used: 7 to 8
weeks old (young group) and 100 to 120 weeks old (aged group). Both the aged and young rats produced on ovalbumin-specific **IgE** antibody and exhibited an immediate asthmatic response after exposure to ovalbumin,
but the degree of specific **IgE** antibody was significantly higher in young rats. The young group showed a marked increase in the number of eosinophils and neutrophils in bronchoalveolar lavage fluid 2 days after exposure to ovalbumin, whereas no eosinophilia was seen in the aged group.
To evaluate the mechanism of the decreased accumulation of eosinophils in aged rats, cells from popliteal lymph nodes from ovalbumin-sensitized rats
were incubated with ovalbumin for 48 hours. Although eosinophil chemotactic activity, determined by a **modified** Boyden chamber method, was present in the supernatant of cultured lymph node cells from young rats, it was absent from those of aged rats. In vivo administration of anti-IL-5 monoclonal antibody revealed that one of the factors of eosinophil chemotactic activity was IL-5. Lymph node cells from aged rats tended to produce greater amounts of **interferon-gamma** than did those from young animals. Findings indicate that aged rats have a
defect in eosinophil accumulation in sites exposed to antigen, probably because of an age-dependent alteration in T cells.

L33 ANSWER 16 OF 30 CAPLUS COPYRIGHT 2001 ACS
1996:756546 Document No. 126:17804 Human antibodies derived from immunized xenomice. Kucherlapati, Raju; Jakobovits, Aya; Klapholz, Sue; Brenner, Daniel G.; Capon, Daniel J. (Cell Genesys, Inc., USA). PCT Int. Appl. WO 9634096 A1 19961031, 64 pp. DESIGNATED STATES: W: AU, CA, FI, HU, JP, KR, NO, NZ; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1995-US5500 19950428.
AB Antibodies with fully human variable regions against a specific antigen can be prepd. by administering the antigen to a transgenic animal which has been **modified** to produce such antibodies in response to antigenic challenge, but whose endogenous loci have been disabled.

Various subsequent manipulations can be performed to obtain either antibodies per se or analogs thereof.

L33 ANSWER 17 OF 30 CAPLUS COPYRIGHT 2001 ACS
1997:2495 Document No. 126:30350 Human antibodies derived from immunized xenomice. Kucherlapati, Raju; Jakobovits, Aya; Klapholz, Sue; Brenner, Daniel G.; Capon, Daniel J. (Cell Genesys, Inc., USA). PCT Int. Appl. WO 9633735 A1 19961031, 69 pp. DESIGNATED STATES: W: AU, CA, HU, JP, KR, NO, NZ; RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1996-US5928 19960429.
PRIORITY: US 1995-430938 19950427.
AB Fully human antibodies against a specific antigen can be prepd. by administering the antigen to a transgenic animal which has been **modified** to produce such antibodies in response to antigenic challenge, but whose endogenous loci have been disabled. Various subsequent manipulations can be performed to obtain either antibodies per se or analogs thereof. Antibodies or monoclonal antibodies to human interleukin 6, tumor necrosis factor .alpha., CD4, L-selectin, gp39, tetanus toxin, PTH-related protein, and interleukin 8 were prepd. in xenomice.

L33 ANSWER 18 OF 30 MEDLINE
96264102 Document Number: 96264102. PubMed ID: 8666423. Limiting dilution
analysis of CD4 T-cell cytokine production in mice administered native versus polymerized ovalbumin: directed induction of T-helper type-1-like activation. Gieni R S; Yang X; Kelso A; Hayglass K T. (Department of Immunology, University of Manitoba, Winnipeg, Canada.) IMMUNOLOGY, (1996 Jan) 87 (1) 119-26. Journal code: GH7; 0374672. ISSN: 0019-2805. Pub. country: ENGLAND: United Kingdom. Language: English.
AB Polarized expression of T-helper type-1 (Th1)- or Th2-like patterns of cytokine production frequently correlates with disease outcome. Previously, we have described the long-lived reciprocal regulation of ovalbumin (OVA)-specific **IgE** (> 95% inhibition) and IgG2a (300-800-fold increased) production following administration of high MW OVA polymers (OVA-POL), in both de novo and ongoing OVA (alum)-induced responses. Here, limiting dilution analysis (LDA) was used to compare precursor frequencies of CD4 T cells producing **interferon-gamma** (IFN-gamma), interleukin-4 (IL-4) or IL-10 following OVA versus OVA-POL exposure in vivo. Adjuvants were not used, so as to circumvent their impact on measurement of precursor frequencies. We found that the two forms of antigen elicited T-cell activation of comparable intensity, as indicated by equivalent precursor frequencies of clonogenic antigen-specific CD4 T cells. However, they elicited qualitatively different cytokine responses. OVA-POL treatment led to 10-fold higher (mean of six independent LDA experiments) frequencies of IFN-gamma-producing cells, and a mean fivefold lower frequency of IL-10-producing cells, than was observed following in vivo administration of unmodified OVA. Thus, the high MW polymerized form of antigen acted to steer commitment of naive (for this antigen) CD4 T-cell activation from a situation in which IL-10 producers outnumbered IFN-gamma-producing cells by a factor of 4:1 (found in mice administered OVA), to one where IFN-gamma producers dominated by a factor of 11:1 (in mice given OVA-POL), i.e. a qualitative shift in the nature of the OVA-specific response induced from Th2-like to Th1-like. In vivo co-administration of anti-IFN-gamma monoclonal antibody (mAb) abolished the capacity of OVA-POL to preferentially elicit Th1-like dominance. Interestingly, although the ratios of IFN-gamma:IL-4 and IFN-gamma:IL-10 OVA-specific precursor frequencies were strongly increased following OVA-POL exposure (mean 18- and 47-fold higher), the frequency of IL-4-producing CD4 T cells did not

differ significantly. The data suggest that this **modified** antigen promotes in vivo commitment of naive T cells towards a Th1-like response, with consequent inhibition of **IgE** and enhancement of IgG2a responses, not through direct effects on IL-4 production, but via decreased frequencies of IL-10 and increased frequencies of IFN-gamma-producing OVA-specific CD4 cells. Collectively, the data (1) demonstrate the ability to manipulate commitment of antigen-driven CD4 T-cell populations in naive mice to specific patterns of cytokine gene expression, and (2) provide in vivo evidence of the regulatory role played by IFN-gamma in limiting induction and/or expansion of IL-4- and IL-10-producing CD4 cells to protein **allergens**.

L33 ANSWER 19 OF 30 MEDLINE
96001963 Document Number: 96001963. PubMed ID: 7582536. Modulation of mite antigen-induced immune responses by lecithin-bound iodine in peripheral blood lymphocytes from patients with bronchial asthma. Kawano Y; Noma T. (Department of Pediatrics, Saitama Medical School, Japan.) BRITISH JOURNAL OF PHARMACOLOGY, (1995 Aug) 115 (7) 1141-8. Journal code:
B00; 7502536. ISSN: 0007-1188. Pub. country: ENGLAND: United Kingdom. Language: English.
AB 1. Dermatophagoides farinae (Df) mite antigen induced **IgE** synthesis associated with an imbalance of cytokine production in mite-sensitive patients with bronchial asthma; increased production of interleukin 4 (IL-4), and decreased production of **interferon-gamma** (IFN-gamma) was specifically induced in these patients' lymphocytes. 2. Lecithin-bound iodine (LBI), with which children with bronchial asthma have been successfully treated in the range of 0.5 to 5 microM, concentrations comparable to LBI blood levels in medicated individuals, **modified** mite antigen-induced immune responses, thereby decreasing abnormal lymphocyte functions. 3. In Df antigen-driven immune responses, inhibition of **IgE** generation accompanied by suppression of IL-4 and the recovery of IFN-gamma production was successful when LBI was used in vitro. 4. LBI also acted on normal PBMCs by downregulating the IL-4-induced **IgE** synthesis, phytohaemagglutin (PHA)- and phorbol myristate acetate (PMA) plus calcium ionophore (CaI)-induced IL-4 secretion, and by upregulating purified protein derivatives (PPD)-induced IFN-gamma production. Therefore, LBI was capable of inhibiting the **IgE** and IL-4 responses and of enhancing IFN-gamma production both from **allergen**-stimulated atopic cells and from non-atopic cells appropriately stimulated. 5. The expression of human histocompatibility leukocyte antigen (HLA), class II antigens and intercellular adhesion molecule 1 (ICAM-1) on monocytes, crucial molecules for T cell-monocyte interactions, was not altered by LBI. 6. LBI probably acts as an immunomodulator to ameliorate mite antigen-induced abnormal cell-mediated immune responses in patients with bronchial asthma caused by Df antigen thereby leading to improvement of their clinical status.

L33 ANSWER 20 OF 30 CAPLUS COPYRIGHT 2001 ACS
1995:607837 Document No. 123:81479 Long-lived inhibition of **IgE** responses and induction of IFN-gamma dominated cytokine synthesis patterns by chemically **modified allergen**. Gieni, Randall Scott (Univ. of Manitoba, Winnipeg, MB, Can.). 219 pp. Avail. NLC From: Diss.
Abstr. Int. B 1995, 55(11), 4777 (English) 1994.
AB Unavailable

L33 ANSWER 21 OF 30 CAPLUS COPYRIGHT 2001 ACS
1994:526198 Document No. 121:126198 Detection of **allergen**- and

mitogen-induced human cytokine transcripts using a competitive polymerase chain reaction. Huang, Shau-Ku; Essayan, David M.; Krishnaswamy, Guha; Yi, Ming; Kumai, Megumi; Su, Song-Nan; Xiao, Hui-Qing; Lichtenstein, Lawrence M.; Liu, Mark C. (The Johns Hopkins Asthma and Allergy Center, 5501 Hopkins Bayview Circle, Baltimore, MD, 21224-6801, USA). J. Immunol. Methods, 168(2), 167-81 (English) 1994. CODEN: JIMMBG. ISSN: 0022-1759.

AB Human cytokines, IL-4, IL-5, and IFN-.gamma. play an important role in the regulation of **IgE** synthesis and atopic diseases. In this communication, the authors describe the development of a quant. assay of steady-state cytokine mRNAs (IL-4, IL-5, and IFN-.gamma.) from a variety of cell sources, including peripheral blood mononuclear cells (PBMCs) stimulated with either a mitogen (PHA) or ragweed pollen **allergen** ext., and cells from **allergen**-challenged inflammatory sites. Quant. anal. of IL-5, IL-4 and IFN-.gamma. transcripts was achieved by a competitive reverse transcription-polymerase chain reaction (RT-PCR) technique using internal std. (IS) cRNAs in the presence of specific oligonucleotide primers. Each IS was generated from a plasmid vector contg. the resp. cytokine cDNA **modified** by insertion with an SV40-DNA fragment. Both test RNA and IS were reverse-transcribed and subjected to the 'competitive' PCR in the same tube. The authors first demonstrate the linearity and reproducibility of this technique; second, the authors apply this competitive PCR assay to analyze quant. the expression of IL-4, IL-5, and IFN-.gamma. transcripts in PBMCs before and after stimulation with PHA or crude ragweed **allergen**. Finally, the authors analyzed cells isolated from the lung lavage fluids of an atopic subject following **allergen** challenge, and showed a significant increase of IL-4 and IL-5 transcripts, but not IFN-.gamma., in the **allergen**-challenged site when compared to the control. This technique of PCR quantitation provides an easy and efficient tool to study the expression of cytokine genes in allergic inflammatory diseases.

L33 ANSWER 22 OF 30 SCISEARCH COPYRIGHT 2001 ISI (R)

93:386372 The Genuine Article (R) Number: LH549. CHEMICALLY-**MODIFIED** ANTIGEN PREFERENTIALLY ELICITS INDUCTION OF TH1-LIKE CYTOKINE SYNTHESIS PATTERNS INVIVO. YANG X; GIENI R S; MOSMANN T R; HAYGLASS K T (Reprint).

UNIV MANITOBA, DEPT IMMUNOL, WINNIPEG R3E 0W3, MANITOBA, CANADA; UNIV ALBERTA, DEPT IMMUNOL, EDMONTON T6G 2H7, ALBERTA, CANADA. JOURNAL OF EXPERIMENTAL MEDICINE (01 JUL 1993) Vol. 178, No. 1, pp. 349-353. ISSN: 0022-1007. Pub. country: CANADA. Language: ENGLISH.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Differential activation of CD4+ T cell subsets in vivo leads to the development of qualitatively different effector responses. We identify an approach that allows selective activation of strongly Th1-dominated immune responses to protein antigens. Whereas in vivo administration of ovalbumin (OVA) induces cytokine synthesis that is neither Th1 nor Th2 dominated, administration of glutaraldehyde polymerized, high relative molecular weight OVA (OA-POL) leads to 20-fold increase in the ratio of **interferon gamma** (IFN-gamma)/IL-4 and IFN-gamma/IL-10 synthesis observed after short-term, antigen-mediated restimulation directly ex vivo. In contrast, concurrent in vivo administration of anti-IFN-gamma mAb and OVA or OA-POL results in marked increases in IL-4 and IL-10, and decreased IFN-gamma production, reflecting a polarization of the response towards a Th2-like pattern of cytokine synthesis. These observations may be useful in clinical settings including hypersensitivity, autoimmune diseases, and vaccine development where the ability to actively select specific patterns of cytokine gene expression

would be advantageous.

L33 ANSWER 23 OF 30 MEDLINE
93384078 Document Number: 93384078. PubMed ID: 7690528. Human in vitro experimental model for CD4+ T cell targeted immunotherapy to house dust mite. O'Hehir R E; Lamb J R. (Department of Immunology, St. Mary's Hospital Medical School, London, England.) ANNALS OF ALLERGY, (1993 Sep) 71 (3) 317-21. Journal code: 4XC; 0372346. ISSN: 0003-4738. Pub. country:
United States. Language: English.
AB CD4+ T cells play a critical role in the initiation and potentiation of the allergic immune response. Development of **allergen**-mediated hyposensitization therapies directed at this cell type requires two key steps: (1) identification of the epitopes that are crucial for activating the T-cell response and (2) definition of the specificity of the HLA-D region molecules that restrict T-cell recognition of these epitopes. We have located the major T-cell determinants of the group II **allergen** of the house dust mite species Dermatophagoides pteronyssinus (Der p II). We have also identified a T-cell clone for which the HLA-DP*0401 allele restricts recognition of the group I **allergen** residues of house dust mite. This clone overproduces IL-4 and IL-5, cytokines that promote **IgE** synthesis. When these cells are rendered nonresponsive by incubation with a supraoptimal concentration of their **allergen** peptide determinant, they lose their ability to secrete IL-4 but maintain **interferon gamma** production. This **modified** pattern favors a switch away from the pathway of **IgE** synthesis to that of IgG synthesis. These findings suggest that the use of selected peptides in vaccines may allow the redirection of allergic immune responses.

L33 ANSWER 24 OF 30 SCISEARCH COPYRIGHT 2001 ISI (R)
93:11982 The Genuine Article (R) Number: KE757. **ALLERGEN**-SPECIFIC MODULATION OF CYTOKINE SYNTHESIS PATTERNS AND **IGE** RESPONSES INVIVO WITH CHEMICALLY **MODIFIED ALLERGEN**. GIENI R S; XI Y; HAYGLASS K T (Reprint). UNIV MANITOBA, DEPT IMMUNOL, 730 WILLIAM AVE, WINNIPEG R3E 0W3, MANITOBA, CANADA. JOURNAL OF IMMUNOLOGY (01 JAN 1993) Vol. 150, No. 1, pp. 302-310. ISSN: 0022-1767. Pub. country: CANADA.
Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Hypersensitivity and **IgE** synthesis are highly dependent on the balance in which production of IL-4 and IFN-gamma is induced. An immunologic approach that alters the dominant pattern of cytokine synthesis and antibody production that is elicited after exposure to native **allergen** is described. High M(r), glutaraldehyde-polymerized OVA administered (i.p.) before or after immunization with unmodified OVA induces greater-than-or-equal-to 95% inhibition of specific **IgE** synthesis concomitant with 300- to 800-fold increases in IgG2a production in C57BL/6 mice. These changes result from a genetically controlled shift in the pattern of cytokine production within the **allergen**-specific T cell repertoire as demonstrated by i) susceptibility of the changes induced upon administration of **modified allergen** to in vivo treatment with anti-IFN-gamma mAb and ii) a 5- to 7-fold increase in the ratio of IFN-gamma:IL-4 synthesis after overnight culture directly ex vivo. This system should prove useful in identification of the factors which are influential in the commitment of T cells to Th1- or Th2-like patterns of cytokine synthesis. Moreover, as defective induction of IFN-gamma by **allergen**-specific T cells appears to play a role in elevated **IgE** synthesis and human allergy, this approach may have

therapeutic potential.

L33 ANSWER 25 OF 30 SCISEARCH COPYRIGHT 2001 ISI (R)
91:581061 The Genuine Article (R) Number: GK972. ANTIGEN-SPECIFIC INHIBITION OF ONGOING MURINE **IGE** RESPONSES .2. INHIBITION OF **IGE** RESPONSES INDUCED BY TREATMENT WITH GLUTARALDEHYDE-**MODIFIED ALLERGENS** IS PARALLELED BY RECIPROCAL INCREASES IN IGG2A SYNTHESIS . HAYGLASS K T (Reprint); STEFURA W P. UNIV MANITOBA, DEPT IMMUNOL, MRC, ALLERGY RES GRP, 730 WILLIAM AVE, WINNIPEG R3E 0W3, MANITOBA, CANADA (Reprint). JOURNAL OF IMMUNOLOGY (1991) Vol. 147, No. 8, pp. 2455-2460. Pub. country: CANADA. Language: ENGLISH.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Administration of high m.w. glutaraldehyde-polymerized OVA (termed OVA-POL) before OVA-[Al(OH)3] immunization of C57BL/6 mice markedly impairs their capacity to generate OVA-specific **IgE** responses, while simultaneously resulting in striking enhancement of Ag-specific IgG2a responses. We demonstrate here that treatment with this class of chemically **modified allergen** also results in pronounced inhibition of ongoing **IgE** responses in vivo. The abrogation of well established murine **IgE** responses that is elicited after treatment with OVA-POL (i) is potent (97%), (ii) is long lived, and (iii) reflects reciprocal regulation of Ag-specific **IgE** and IgG2a responses in vivo. Moreover, the capacity of OVA-POL-treated mice to generate secondary **IgE** responses remains strongly decreased for at least 260 days and six subsequent immunizations with native **allergen**, despite there being no further treatment with **modified allergen**. These changes in **IgE** and IgG2a responsiveness are Ag specific and T cell dependent.

L33 ANSWER 26 OF 30 MEDLINE
92010015 Document Number: 92010015. PubMed ID: 1717367. Long-lived reciprocal regulation of antigen-specific **IgE** and IgG2a responses in mice treated with glutaraldehyde-polymerized ovalbumin. Hayglass K T; Gieni R S; Stefura W P. (MRC Group for Allergy Research, Department of Immunology, University of Manitoba, Winnipeg, Canada.) IMMUNOLOGY, (1991 Aug) 73 (4) 407-14. Journal code: GH7; 0374672. ISSN: 0019-2805. Pub. country: ENGLAND: United Kingdom. Language: English.
AB Previously, we discovered that administration of high Mr glutaraldehyde-polymerized ovalbumin (OA) to C57BL/6 mice prior to immunization with OA in Al(OH)3 adjuvant resulted in induction of an **interferon-gamma** (IFN-gamma) dependent, split tolerance in which maximal OA-specific **IgE** responses were 1-3% of those observed in saline-treated OA-[Al(OH)3] immunized controls. Concomitantly, these mice exhibited up to 10(3)-fold increases in OA-specific IgG2a synthesis. In this report we examine the longevity and resilience of these reciprocal effects on **IgE** inhibition/IgG2a enhancement over extended periods of time and following multiple re-exposures to the sensitizing **allergen**. The data indicate that the T-cell mediated changes in responsiveness which are induced upon exposure to glutaraldehyde-**modified** protein **allergen**, but not unmodified **allergen**, are (i) extremely long-lived (greater than 350 days); (ii) resistant to at least five re-immunizations with OA in Al(OH)3 adjuvant; and (iii) antigen-specific. The results are consistent with a virtually permanent shift in the OA-specific T-cell repertoire in vivo from one dominated by Th2-like patterns of cytokine synthesis (IL-4) to one dominated by Th1-like (IFN-gamma) cytokine production.

L33 ANSWER 27 OF 30 MEDLINE
91108324 Document Number: 91108324. PubMed ID: 1703203. Anti-**interferon gamma** treatment blocks the ability of glutaraldehyde-polymerized **allergens** to inhibit specific

IgE responses. HayGlass K T; Stefura B P. (Department of Immunology, University of Manitoba, Winnipeg, Canada.) JOURNAL OF EXPERIMENTAL MEDICINE, (1991 Feb 1) 173 (2) 279-85. Journal code: I2V; 2985109R. ISSN: 0022-1007. Pub. country: United States. Language: English.

AB The lymphokines interleukin 4 and **interferon gamma** (IFN-gamma) have been shown to play an important role in regulation of polyclonal immunoglobulin E (**IgE**) and IgG2a responses in vitro and in vivo. We demonstrate here that treatment with chemically **modified** ovalbumin (OA) results in long-lived, 97-99% inhibition of **allergen**-specific murine **IgE** responses and 10(3)-10(4)-fold increases in anti-OA IgG2a. Responses to unrelated antigens are not affected. Treatment with unmodified OA under the same conditions fails to inhibit primary or secondary **IgE** responses or to increase IgG2a but does lead to pronounced increases in OA-specific IgG1 production. Glutaraldehyde-polymerized ovalbumin (OA-POL)-induced changes in **IgE** and IgG2a responses are abrogated by in vivo treatment with purified monoclonal anti-IFN-gamma antibody (XMG 1.2), a finding indicative of preferential IFN-gamma production upon exposure to chemically **modified**, but not native, **allergen**. The results suggest the possibility that the pattern of cytokine synthesis elicited after exposure to protein antigens, and the resulting immune response, may be dependent upon the form of antigen to which the individual is exposed and consequently may be subject to manipulation.

L33 ANSWER 28 OF 30 MEDLINE

91257889 Document Number: 91257889. PubMed ID: 1710602. Antigen-specific modulation of murine **IgE** and IgG2a responses with glutaraldehyde-polymerized **allergen** is independent of MHC haplotype and Igh allotype. Hayglass K T; Stefura W. (Dept. of Immunology, University of Manitoba, Winnipeg, Canada.) IMMUNOLOGY, (1991 May) 73 (1) 24-30. Journal code: GH7; 0374672. ISSN: 0019-2805. Pub. country: ENGLAND: United Kingdom. Language: English.

AB C57BL/6 mice treated with high Mr, glutaraldehyde-polymerized ovalbumin of highly restricted heterogeneity (termed OVA-POL) exhibit **IgE** responses upon later exposure to unmodified OVA which, at peak, are 1-3% of those observed in untreated controls. Concomitantly, anti-OVA IgG2a responses are elevated 250-1000-fold via an **interferon-gamma** (IFN-gamma)-dependent mechanism (ref. 4). Here, the impact of OVA-POL treatment on antigen-specific primary and secondary **IgE** responses is examined in 14 strains of mice. The data indicate that the capacity of this **modified allergen** to induce pronounced inhibition of **IgE** responses (75-99%), paralleled by up to 1000-fold increases in IgG2a responses, is not genetically restricted. Moreover, these changes in antibody production were (i) antigen-specific, (ii) isotype-specific and (iii) operated independently of the responder status, MHC or Igh haplotype of the responder mice. In contrast, treatment with unmodified OVA under the same conditions was without effect on **IgE** production and led to minor increases in anti-OVA IgG2a production.

L33 ANSWER 29 OF 30 MEDLINE

90316167 Document Number: 90316167. PubMed ID: 2142456. **Allergen**-directed expression of Fc receptors for **IgE** (CD23) on human T lymphocytes is modulated by interleukin 4 and **interferon-gamma**. Prinz J C; Baur X; Mazur G; Rieber E P. (Institute for Immunology, Ludwig-Maximilians-University, Munich, FRG.) EUROPEAN JOURNAL OF IMMUNOLOGY, (1990 Jun) 20 (6) 1259-64. Journal code: EN5; 1273201. ISSN: 0014-2980. Pub. country: GERMANY, WEST: Germany, Federal Republic of. Language: English.

AB T lymphocytes bearing Fc receptors (FcR) for immunoglobulins are known to have immunoglobulin class-specific regulatory functions. Here we report that expression on T cells of the low-affinity FcR for **IgE** (Fc epsilon RII/CD23) is preferentially induced by stimulation with antigens that cause an **IgE** response. T cells from eight patients allergic to the hemoglobin of Chironomus thummi thummi mosquito larvae (CHIT I) were analyzed for reactivity with the anti-FcERII/CD23 monoclonal antibody (mAb) M-L25 under various conditions. No Fc epsilon RII/CD23+ T cells were observed among freshly isolated, resting peripheral blood mononuclear cells (PBMC). Stimulation of PBMC with CHIT I, however, induced a marked although transient Fc epsilon RII/CD23 expression on a large portion of the **allergen**-activated T lymphocytes. It reached a maximum of 37.2 +/- 4.6% Fc epsilon RII/CD23+ T cell blasts on day 5 of culture. The selectivity of this expression became evident when compared to non-allergenic control antigens: after stimulation of PBMC with tetanus toxoid or purified protein derivative from tuberculin a maximum of 4.6% +/- 1.4% and 4.2% +/- 1.1% T cell blasts was found to express Fc epsilon RII/CD23, respectively. Activation by an anti-CD3 mAb was insufficient to induce Fc epsilon RII/CD23 on T cells. The **allergen**-stimulated Fc epsilon RII/CD23+ T cells exclusively belonged to the CD4+CD29+ helper inducer T cell subset. Using a cDNA probe coding for the B cell Fc epsilon RII/CD23, Northern blot analysis revealed a 1.7-kb Fc epsilon RII/CD23 mRNA in extracts of highly purified **allergen**-stimulated T cells. It was of the same size as Fc epsilon RII/CD23 mRNA of the lymphoblastoid B cell line WI-L2. Of several cytokines tested [interleukin (IL) 1 to IL 6, **interferon-gamma** (IFN-gamma), tumor necrosis factor-alpha] only IL 4 and IFN-gamma significantly **modified allergen**-induced Fc epsilon RII/CD23 expression on T cells. The latter was enhanced nearly twofold in the presence of IL 4, and was almost completely abrogated by IFN-gamma. IL 4, however, could not increase the number of Fc epsilon RII/CD23+ T lymphocytes either alone or in combination with an anti-CD3 mAb. Taken together, the selective induction of Fc epsilon RII/CD23 on T cells by **allergen** and its inclusion in the regulatory network of cytokines point to an important role of Fc epsilon RII/CD23+ T lymphocytes in the human **IgE** response.

L33 ANSWER 30 OF 30 BIOSIS COPYRIGHT 2001 BIOSIS
1991:66178 Document No.: BA91:34838. ISOTYPE-SELECTIVE ABROGATION OF ESTABLISHED **IGE** RESPONSES. HAYGLASS K T; STEFURA W. DEP. IMMUNOLOGY, UNIVERSITY MANITOBA, 730 WILLIAM AVENUE, WINNIPEG, MANITOBA R3E 0W3, CAN.. CLIN EXP IMMUNOL, (1990) 82 (3), 429-434. CODEN: CEXIAL. ISSN: 0009-9104. Language: English.

AB Chemically **modified allergens** have been extensively studied in an attempt to develop materials of increased efficacy and improved safety for use in the immunotherapy of allergic disease. Most of the strategies that have been developed yield products that strongly inhibit de novo **IgE** responses but have only marginal impact on ongoing **IgE** responses. We report the virtual abrogation of pre-established murine anti-ovalbumin **IgE** responses using a glutaraldehyde-polymerized ovalbumin preparation (OA-POL) of Mr 3 .cntdot. 5 .times. 107. Secondary **IgE** responses are inhibited by 97-99% over a period of at least 8 months following three i.p. course of OA-POL treatment. Administration of five additional ovalbumin [Al(OH)3] booster immunizations over this period fails to alter this unresponsive state. The inhibition of antigen-specific **IgE** responses is isotype specific.

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